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THE BRITISH JOURNAL OF TUBERCULOSIS AND DISEASES OF THE CHEST

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NOTICE TO CONTRIBUTORS

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BRITISH JOURNAL OF TUBERCULOSIS
AND DISEASES OF THE CHEST

Vol. L. APRIL, 1956 No. 2.

THE SURGICAL TREATMENT OF SKELETAL TUBERCULOSIS: AN ANALYSIS OF RESULTS

BY J. TRUETA, E. M. SHIPSEY AND A. TRIAS

From the Nuffield Orthopædic Centre, Oxford

THE management of skeletal tuberculosis is being influenced by antibiotics in a way which is as yet not well defined. In the past it was agreed that bone and joint tuberculosis presented a number of pathological and therapeutic features of its own, among them the metastatic nature of the disease—it being secondary to a pre-existing tuberculous lesion, usually of the lymphatic system —and the slow process by which the bone focus becomes first circumscribed, later restricted by fibrosis, subsequently calcified and eventually ossifies again. In common with the other forms of secondary tuberculosis the behaviour of the skeletal focus depends in a large measure on the systemic disorder caused by the tuberculous toxins lowering the "general resistance" of the patient to the disease. Thus for the last fifty years or more the treatment of skeletal tuberculosis has had a twofold objective, namely (*a*) to improve the general condition of the patient by measures which would limit the lymphatic invasion, and (*b*) to control the local lesion by fulfilling a set of principles directed to protect the healing mechanism in the focus. Open-air treatment, immobilisation of the affected limb and even arthrodesis must be considered as parts of this programme.

In the majority of classic works on skeletal tuberculosis (Sorrel and Sorrel-Dejerine, 1932; Girdlestone, 1940) due emphasis is placed on the prevention of sinuses through which the ordinary contaminants (staphylococcus, streptococcus, pyocyaneus, *B. coli*, etc.) may reach the tuberculous focus and disturb its tendency to heal. Thus the care of the abscesses and their covering skin, as much as immobilisation, counted among the measures to protect the skeletal focus.

When enough streptomycin was made available for the treatment of tuberculous patients it was interesting to evaluate the part that this, and subsequently other substances also, would play in controlling the general disease and that of the infected bone or joint. Would the new agent shorten the period of general illness and thus allow the advancement of the date of any operation indicated? Would it in any way accelerate the healing of the local skeletal lesion? If the protection offered by streptomycin against the circulating Koch bacillus was great enough, would its use allow greater surgical enterprise to eradicate the walled-in or perhaps even the invasive focus and thus cause the patient to revert to the *status quo ante*?

(*Received for publication August* 2, 1955.)

All these questions awaited an answer before attempting any substantial modification of the well-established management of skeletal tuberculosis as practised in the specialised centres of this and some other countries. A circumstantial fact influenced a number of orthopædic surgeons—amongst them one of the authors (J.T.)—in no small way in planning the study of the rôle of streptomycin, PAS and later Isoniazid in the treatment of orthopædic tuberculosis. This fact was the chronological order in which the first antibiotics were discovered, streptomycin appearing when the trials on penicillin were reaching conclusion (Hirsch, 1951). The experience already accumulated by then in the treatment of acute and chronic osteomyelitis (Agerholm and Trueta, 1946; Trueta, 1951) influenced the early decision to study the merits of streptomycin in protection against tuberculous dissemination following surgical interference with the skeletal lesion (Wilkinson, 1950; Orell, 1951).

The possibility that at last the focus could be removed was particularly appealing, for it had become well recognised that either the spontaneous or the surgical opening of the tuberculous focus was full of danger. This is exemplified by the phrase of Calot (1915) " to open an abscess of a tuberculous spine or to permit it to burst, is to open a door through which death almost always enters." Repeated failures, many amounting to catastrophes, had taught the surgeon to be conservative and surgery was only indicated when the disease was quiescent and usually in order to stiffen the joints by arthrodesis. Only in exceptional and small series was radical surgery followed by successful results (Ito *et al.*, 1934; Erlacher, 1935). Secondary infections, however, following sinuses and tuberculous dissemination causing miliary spread, meningitis and new bone foci soon curtailed surgical enterprise.

In 1949 enough streptomycin was available to allow us to make a systematic study of its rôle in the treatment of skeletal tuberculosis and to control the acute forms of the disease (Riggins and Hinshaw, 1949). Our previous experience with penicillin prompted us from the beginning to plan the removal of the skeletal focus wherever possible and as soon as its localisation and the general condition of the patient would allow. The prevention of dissemination was the task assigned to streptomycin and PAS after the removal of the focus and the isolating wall which had prevented the blood from reaching it.

The present work is the first evaluation of our results after six years' experience. In the meantime a number of reports on results have been published (Wilkinson, 1954; Felländer, 1955). We now consider that sufficient time has elapsed to judge the changes in the management of skeletal tuberculosis which the administration of the antibiotics is bringing about.

Material

The present analysis includes 38 patients with 42 skeletal tuberculous foci, all of them treated with streptomycin and some other substance such as PAS and INH, in association with surgery directed at the removal of the focus affecting the locomotor system.

For the purpose of analysis the cases have been grouped in two main sections: (1) patients suffering from a focus primarily or exclusively affecting the skeletal tissues; (2) cases affected by tuberculosis of the soft tissues involving or not the adjacent bone such as in trochanteric bursitis. To allow a closer

scrutiny of results, section one has been subdivided into two groups in accordance with the type of operation performed. Group *a* had excision or curettage of the tuberculous focus aiming at the preservation of movement (17 cases); Group *b* had excision or curettage of the tuberculous focus or joint followed by arthrodesis (11 cases). Section 2 has also been subdivided into two; Group *a* comprises those with excision of the soft tissues only (9 cases) and Group *b* those with excision or curettage of the trochanteric focus only (5 cases). Apart from the surgery and antibiotics, all the patients had the same basic management which until now has been recognised as essential for the treatment of skeletal tuberculosis such as immobilisation—usually on a frame—open air treatment, vitamins, etc. The factors analysed in each case were age, sex, time of illness before antibiotic treatment was initiated, abscesses, sinus, details of antibiotic therapy, surgical treatment, healing time of the surgical wound, time of post-operative immobilisation, and finally the period of follow-up until the clinical and radiographic restoration of the region affected by the disease. The basis for judgment of the results was provided by the clinical, radiographic and laboratory data at our disposal.

We are conscious of the uncertainty of any conclusion based on the study of so small a number of cases, but we have preferred to observe a restricted number of patients closely and to follow them up individually for as long a period of time as possible than to base our study on large groups where the individual case is lost in the statistical approach of a mass survey.

Amongst all the patients treated there was one death (39), which needs to be considered first, as the treatment does not correspond to the criteria established for the selection of cases; this was a case with tuberculosis of the foot, hip and greater trochanter with sinuses, who had been affected for more than 30 years and was seriously ill at the time of excision of a trochanteric bursa. She died of an allergic reaction following the administration of streptomycin. At necropsy a destructive tuberculosis of both suprarenals was found. The case was operated upon as a life-saving measure and not, as in the rest of the cases, to eradicate the active focus. Nevertheless, it must be included among this series of excised tuberculous foci.

Patients and lesions

A "radical" removal of the tuberculous lesion by excision or curettage has been performed in 42 foci in 38 patients. One had three separate foci (11, 12, 31) in the wrist, ankle and trochanteric bursa. The first two lesions were operated on simultaneously. The trochanteric bursa, which was excised two years later, was presumably infected in the same hæmatogenous spread, although with a different time of evolution.

Two further patients showed two skeletal localisations each, which were operated on; in the first case (33, 34) both hips and in the second (24, 25) the lower end of the tibia and the os calcis of the same leg.

(*a*) Thirteen patients had only one detectable tuberculous lesion (37 per cent.).

(*b*) Twenty-five (63 per cent.) patients presented among them 46 tuberculous lesions, 27 orthopædic and 19 visceral, 4 of which were renal (7, 15, 18, 20), comprising almost 10 per cent. of all the patients. In all, there are

88 lesions in 38 patients, an average of slightly more than 2 lesions for every patient.

Follow-up

The follow-up period for each lesion varies between 1 and just over 6 years; the average is 3 years.

Less than 2 years	9
From 2 to 3 years	9
From 3 to 4 years	10
From 4 to 5 years	8
From 5 to 6 years	4
More than 6 years	1

1 died 36 days after operation.

Diagnosis

Of the 42 foci, 38 had laboratory evidence of tuberculous infection obtained either by histology, culture of pus from the focus, guinea-pig inoculation, gland biopsy or by more than one of these procedures.

In 4 foci no direct proof of tuberculosis was obtained, but in 3 (4, 14 and 21) other foci were present from which evidence of tuberculosis was collected. Only one patient cannot be considered absolutely characteristic (4) in spite of the fact that the clinical history and evolution to the time of operation was similar to that of a tuberculosis of a femoral neck. The post-operative course of the lesion so closely resembled that of other cases of proven tuberculosis that we have included it with the others.

Antibiotic Treatment

Of the 42 lesions 35 were treated with antibiotics before and after the operation for three months or longer (Group 1). Seven lesions had antibiotics only to cover the operation period (Group 2). Four lesions had no antibiotics (Group 3), one of them due to a wrong diagnosis of rheumatoid arthritis being made. They were useful as unsuspected controls but are not included amongst the 38 cases in the series.

Nature of the antibiotic

Streptomycin (0·25 to 1·0 g. daily depending on age) associated with PAS (5 to 20 g. daily) was administered in 36 instances. Streptomycin and INH (50 mg.) three times a day was given to four adults. In 2 instances only streptomycin was used.

Results

The results have been divided into very good, good, poor or failure.

Very Good

1. Restoration of bone and joint structures.
2. Closure of all sinuses.
3. Total absence of pain.
4. Solid surgical fusion when attempted or retention of 75 per cent. or more of active joint motion.
5. Restoration of general health.

Good

1. Cessation of bone and joint damage.
2. Closure of all sinuses.
3. Total absence of pain.
4. Retention of 25 to 75 per cent. of active joint motion.
5. Temporary recurrence of slight discharge.
6. Improvement of general condition.

Poor or Failure

When any of the above conditions were absent.

Comparing the results of treatment in the two groups of patients who had single lesions (Group *a*) or associated lesions (Group *b*) it was noted that when there were associated lesions the results were better (very good=81 per cent.; poor and the death=19 per cent.) than when there were no associated lesions (very good and good 73 per cent. and poor 27 per cent.).

Sex—19 males. 19 females.
Age—This series includes patients from 18 months to 65 years.

					Per cent.
(*a*)	0-25 years	19 lesions (45 per cent.)	Very good	10 cases	52·7
			Good	7 „	36·8
			Poor	2 „	10·5
(*b*)	25-65 years	23 lesions (55 per cent.)	Very good	6 cases	26
			Good	7 „	55
			Poor	5 „	22

Success slowly decreases with advancing age; very good results diminish from 52·7 per cent. to 26 per cent., while the poor results increase from 10·5 per cent. to 22 per cent. The whole of the very good and good results also decrease, from 89·5 per cent. and 78 per cent.

Duration of Tuberculous History before Operation

The duration of tuberculous history before the operation varied enormously amongst the 42 foci. The shortest history was of one month, and the longest 32 years (case that died). They were divided into three groups according to the duration of the history and correlating them with the results.

		Per cent.
(1) Of less than 1 year 8 foci (19 per cent.)	Very good and good	100
	Poor	0
(2) Of less than 5 years 18 foci (43 per cent.)	Very good and good	88·8
	Poor	11·2
(3) Of more than 5 years 16 foci (38 per cent.)	Very good and good	68·7
Of which 6 have a history of 20 years or more	Poor	31·3

From this analysis it appears that the earlier the case is surgically treated the better is the result.

Abscesses and Sinuses before Operation

Twenty-five cases (60 per cent.) presented abscesses, sinus or both before the operation. Of these, 5 had a sinus and abscess, 5 a sinus only and 15 an abscess only.

The 38 cases of these series have been divided into three groups according to whether they had complications before the operation or not and also according to the type of complication. The post-operative results are as follows:

				Per cent.
(1)	Without sinus or abscess 17 foci	Results {Very good and good	14	83
		Results {Poor	3	17
		Post-operative complications	3	17
(2)	With abscess only 15 foci	Results {Very good and good	13	86·7
		Results {Poor	2	13·3
		Post-operative complications	4	26·7
(3)	With sinus 10 foci	Results {Very good and good	7	70
		Results {Poor	3	30
		Post-operative complications	3	30

Post-operative complications ranging from simple delay in healing of the wound to temporary or persistent sinus increase with previous abscess and even more so with a previous sinus.

Operations

In this analysis the cases have been grouped according to the nature of the surgical treatment they received. All the cases had in common the fact that the incision was closed by silk sutures. The presence of an abscess, sinus or both was not considered a contraindication for operation.

Section I

(A) *Curettage of the tuberculous focus, primarily or exclusively affecting the bone tissues, aiming at the preservation of movement*

In all cases the curettage of the bone foci was as radical as possible (Figs. 1 and 2). In a number of cases the cavity was packed with bone bank chips (6, 7 and 9) (Figs. 3 and 4).

The localisation of the foci was as follows:

	Cases
Pubis	1
Lower end of femur	1
Ankle region	3
Humeral head	2
Femoral neck	4
Distal end of radius	1
	12

Excision of the tuberculous joint aiming at the preservation of movement

In these the joint was excised and physiotherapy started as soon as possible, aiming at the preservation of movement. In the hip the Girdlestone operation (pseudarthrosis) has been performed in 3 cases.

	Cases
Hip	3
Elbow	2
	5

(B) *Excision or curettage of the tuberculous focus or joint followed by arthrodesis*

	Cases	
Spine	2	(1 laminectomy and 1 costo-transversectomy)
Sacro-iliac	2	
Ankle	5	
Shoulder	2	
	11	

SECTION II

(A) *Excision of the soft tissue only*

An excision of the soft tissue has been performed:

	Cases	
Knee	2	1 synovectomy 1 excision of soft tissue abscess
Trochanteric bursitis	2	
Subdeltoid bursitis	1	
Excision of hip abscess	3	
Tenosynovitis of wrist	1	
	9	

(B) *Curettage of the Trochanteric Focus*

Curettage of the greater trochanter has been done five times.

Healing Time of the Surgical Wounds

Of the 42 wounds 20 healed without delay within the first 14 days; 9 wounds had some delay in healing. In 13 cases, in which the operated extremity was covered by plaster, the wound was found to be soundly healed 20-30 days after the operation, when the plaster was removed, but it was impossible then to state the exact healing time.

The existence of a sinus was recorded when the wound was found either not healed within the normal time or when it was still open at the removal of the plaster. Nine wounds had some delay in healing; 3 developed a sinus immediately after the operation, 6 developed a hæmatoma which was aspirated, but in 2 cases a sinus developed afterwards. It is to be noted that 21 per cent. of the surgical wounds had some delay in healing, but of these only 12 per cent. were left with a sinus. Several authors have already pointed out the importance

of complete hæmostasis when operating on these cases in order to prevent complications.

Cases with hæmatoma .. .. 6 (3, 15, 35 and 42) (with a sinus 38 and 41)
Cases with a sinus .. .. .. 3 (10, 27 and 30)
(See Figs. 1, 2, 3, 4.)

Complications

The local and general complications are considered separately.

I. *Local Complications: Post-operative Sinus*

Eight cases developed a sinus after the operation, two of these are still discharging at the time of writing this report. In one case (38) it seems that the sinus is due to a cavity remaining in a completely ankylosed hip. The second case (41) has a discharge from vertebral lesions.

Three other wounds did not heal by first intention (10, 27 and 30) and had a sinus for 3, 6 and 7 months.

In three cases, after a normal healing of the surgical wound, a sinus broke down temporarily (14, 8 and 12).

These local complications seem to have been favoured by (1) a post-operative hæmatoma, (2) abscesses and sinus before operation, (3) insufficient antibiotic treatment.

II. *General Complications: Intolerance to Antibiotics*

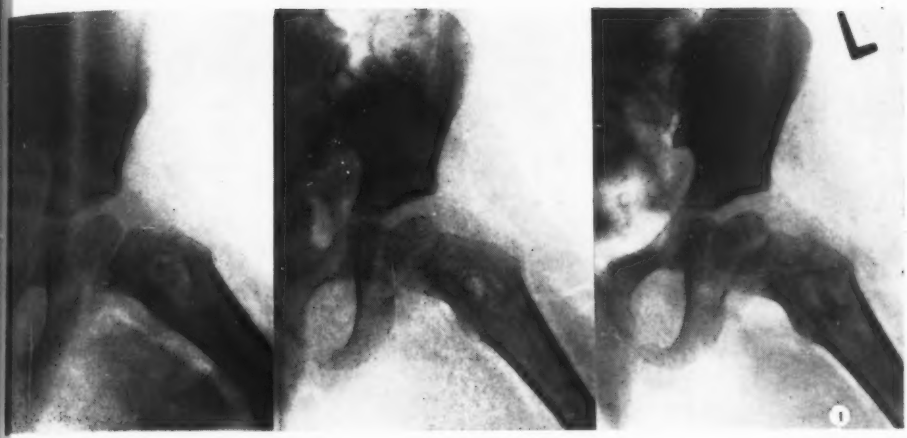
We have had 7 cases of intolerance to antibiotics which can be divided into two groups:

(A) *Intolerance to PAS.* This has been manifested by digestive troubles, sickness, diarrhœa and vomiting (17-40), but only in one case did the PAS have to be discontinued after 35 days (50).

(B) *Intolerance to Streptomycin.* This occurred more often. One case (6) that had a rash of urticarial type had streptomycin discontinued for two weeks. In 3 other cases, deafness appeared at the end of a 3-month course of streptomycin (15, 19 and 30) but has persisted only in one case.

In this series 6 cases had mild general complications and one case has a permanent disability caused by the treatment.

	SECTION I		*SECTION II*		*TOTAL*	*SECTION III* (*without antibiotics*)
	A	B	A	B		
Very good	7	5	3	1	16-40% } 83%	2-50%
Good	7	6	5	1	19-43% } Satisfactory	
Poor	3		1	2	6-14·6% } 17%	2-50%
Dead				1	1- 2·7% } Failures	
Total					42-100%	



(*a*) (*b*) (*c*)

FIG. 1.

Proven tuberculosis of the neck of femur in a girl of 2½ years of age.

(*a*) Cavity occupying more than half the circumference of the neck. Radiograph obtained on 22.9.49 shortly before operation.

(*b*) Progress shown on 3.1.50.

(*c*) 3.5.50.

(*a*) (*b*) (*c*)

FIG. 2.

Same patient as Fig. 1.

(*a*) One year after the curettage-excision (5.9.50).

(*b*) 31.7.52.

(*c*) No residual changes could be detected more than five years after operation (19.10.54).

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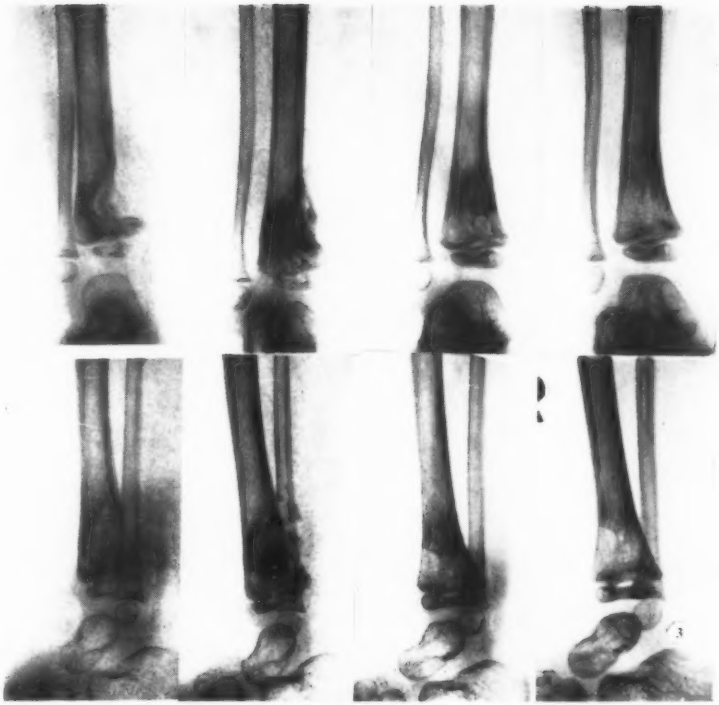

(*a*) (*b*) (*c*) (*d*)

FIG. 3.—Extensive proven tuberculosis occupying almost the whole of the lower tibial metaphysis of a girl (age 2).

(*a*) A.P. and lateral radiograph obtained on 19.3.52, shortly before the curettage-excision.

(*b*) Showing the cavity filled by bone chips. (7.5.52.)

(*c*) 16.9.52.

(*d*) 10.3.53.

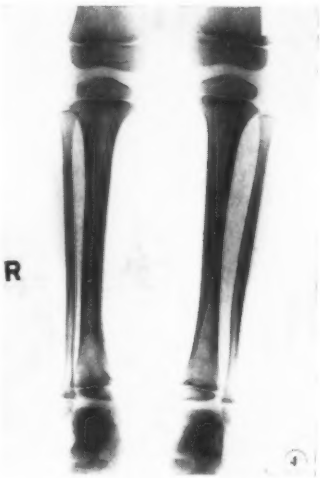

FIG. 4.—The same patient as in Fig. 3 showing complete reintegration of bone structure on 26.10.54, more than 2½ years after operation. Note that the right tibia (the affected one) is slightly shorter than the other.

In 27 cases (64 per cent.) preservation of movement was intended. Of these 17 have a full range of movement, 8 have less than 75 per cent. of normal movement, and 2 less than 25 per cent. of normal movement.

In 11 cases (26 per cent.) an arthrodesis was performed. In 3 other cases the joint was already ankylosed at operation and 1 case died 27 days after operation.

Discussion

From the present analysis it may be inferred that " radical " surgery has acquired a place in the treatment of skeletal tuberculosis. Some points seem to emerge which will probably influence the general management of skeletal tuberculosis. In the first place it is interesting to note that contrary to the old established rule, success in the treatment seems not only related to the age of the patient, the younger the better, but to the duration of the tuberculous history before operation, the shorter the better. A 100 per cent. success was obtained among the cases operated before one year of the infection, while only 68 per cent. success was achieved in cases affected for more than five years. The presence of a pre-operative sinus brought up the number of failures from 17 per cent. to 30 per cent.

Streptomycin associated to PAS used for three months or more gave the best results. When given only to cover the operation the results were more modest and when, as in a group of 4 cases, which are not included in this series, it was not used at all, 2 of the cases were failures.

In the present study we have not included patients with skeletal tuberculosis treated by antibiotics and chemotherapy without " radical " surgery. One of the authors (J.T.) is at present publishing his observations on the very moderate success obtained in a number of patients with Pott's disease in whom enormous doses of streptomycin by several routes were injected in order to control a concomitant tuberculous meningitis. The betterment in the results obtained in the present series seems to be due to the association of early surgery and antibiotics.

Conclusions

1. Streptomycin and chemotherapy have favourably changed the prognosis in skeletal tuberculosis.

2. The main factor responsible for the increased success is the surgical removal of the barriers to the diffusion of the antibiotics from the blood stream. Reciprocally, the antibiotics protect the patient from post-operative complications.

3. The best results were obtained by " radically " removing para-articular foci in the bone with which, without exception, all the patients were cured and the joints preserved.

4. The operation should be performed as soon as the focus has been well localised both clinically and by radiography; nevertheless the patient must have streptomycin and the other anti-tuberculous substances for at least one month pre-operatively.

5. The antibiotic treatment must be continued for at least three months.

6. We are under the impression that the local use of streptomycin at the time of operation has favourably influenced the post-operative course.

7. We cannot as yet dispense with the basic principles of general treatment as established by our teachers.

It will be noted that in this series there is no case of " radical " surgery applied to the spine. We are still uncertain as to the merits or otherwise of the curettage-excision of vertebral bodies in spite of the favourable reports submitted by several authors. The severity of the operation when more than one vertebra is affected, the poor quality of the bed to be filled with bone chips after removing the necrotic tissue, and, last but by no means least, the high percentage of successes that attends the classic method of treatment, has made us cautious on this subject. Of course, the above reservations do not apply to those old cases of spinal tuberculosis with chronic abscesses maintained by large sequestra in the vertebral body. In this, as in chronic osteomyelitis, the only way to help revascularisation is removal of the dead and dying bone.

We would like to thank all our colleagues of the Nuffield Orthopædic Centre for the facilities given to us for the present analysis.

(*Detailed tables appear on the five pages following*)

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SECTION I

Tuberculous Focus, Primarily or Exclusively Affecting the Skeletal Tissues

Group A.—Curettage of the Tuberculous Focus, aiming at the Preservation of Movement

No. of focus	*Age yrs.*	*Sex*	*Duration before opn.*	*Abscess*	*Sinus*	*Anti-biotic group*	*Anti-biotic used*	*Days before opn.*	*Locally*	*Days after opn.*	*Type of opn.*	*Diag. confirmed by*	*Healing time of wound*	*Time of immobili-sation*	*Follow-up*	*Result*
1	6	M	3 yrs. 6 mths.	Yes	No	II	Strept. PAS	10	No	23	Curettage rt. lower fem. focus	Hist.	11 dys.	2 mths.	3 yrs. 6 mths.	Poor
2	5	F	3 mths.	Yes	No	I	Strept. PAS	30	Yes	60	Curettage of pubis	Cult.	16 dys.	9 mths.	4 yrs. 7 mths.	Very good
3	24	F	6 yrs.	No	No	I	Strept. Rimif.	No	No	90	Curettage hum. head	Hist. Cult.	20 dys.	44 dys.	2 yrs.	Poor
4	21	F	2 yrs.	No	No	I	Strept. PAS	90	Yes	90	Curettage hum. head	Clin.	20 dys.	5 mths.	2 yrs. 4 mths.	Very good
5	3	M	3 mths.	No	No	I	Strept. PAS	37	Yes	90	Curettage fem. neck	Clin. Radiol.	15 dys.	3 mths.	2 yrs. 7 mths.	Very good
6	6	F	6 mths.	No	No	I	Strept. PAS	90	Yes	90	Curettage fem. neck bone chips	Cult. Hist. Biop.	10 dys.	9 mths.	1 yr. 9 mths.	Very good
7	4	M	1 yr. 2 mths.	Yes	No	I	Strept. PAS	90	Yes	60	Curettage fem. neck bone chips graft	Hist. Cult.	30 dys.	9 mths.	1 yr. 9 mths.	Very good
8	3	F	3 mths.	No	No	I	Strept. PAS	10	Yes	67	Curettage fem. neck	Cult.	12 dys.	1 yr.	6 yrs.	Very good

SECTION I

Group A.—Curettage of the Tuberculous Focus, aiming at the Preservation of Movement (continued)

No. of focus	*Age yrs.*	*Sex*	*Duration before opn.*	*Abscess*	*Sinus*	*Anti-biotic group*	*Anti-biotic used*	*Days before opn.*	*Locally*	*Days after opn.*	*Type of opn.*	*Diag. confirmed by*	*Healing time of wound*	*Time of immobili-sation*	*Follow-up*	*Results*
9	1½	F	4 mths.	Yes	No	I	Strept. PAS	90	Yes	15	Curettage low. tib. met., bone chips	Hist. Cult. Inoc.	30 dys.	6 mths.	3 yrs.	Very good
10	29	F	8 yrs.	No	Yes	I	Strept. PAS	90	No	22	Curettage rt. lat. mall	Cult.	3 mths.	6 mths.	4 yrs. 2 mths.	Good
11	23	M	2 yrs.	No	No	I	Strept. PAS	90	No	90	Curettage rt. lat. mall	Hist. Cult.	10 dys.	1 yr.	5 yrs.	Good
12	23	M	2 yrs.	No	No	I	Strept. PAS	90	No	90	Curettage rt. rad. styloid	Hist. Cult.	30 dys.	3 mths.	5 yrs.	Good
13	54	F	24 yrs.	No	No	I	Strept.	30	Yes	57	Excision of hip	Hist.	13 dys.	30 dys.	4 yrs. 10 mths.	Poor
14	40	M	29 yrs.	No	No	I	Strept. PAS	5	Yes	87	Pseud. hip	Clin. Radiol.	14 dys.	1 mth.	3 yrs. 3 mths.	Good
15	65	M	3½ yrs.	Yes	No	I	Strept. IHN	90	Yes	13	Excision of hip	Cult.	13 dys.	3 mths.	2 yrs. 8 mths.	Good
16	41	M	7½ yrs.	Yes	Yes	I	Strept. PAS	30	Yes	60	Excision elbow	Cult.	13 dys.	30 dys.	1 yr. 3 mths.	Good
17	58	M	11 yrs.	No	No	I	Strept. PAS	3	Yes	84	Excision elbow	Hist.	30 dys.	30 dys.	1 yr. 7 mths.	Good

SECTION I

Group B.—Curettage of the Tuberculous Focus or Joint followed by Arthrodesis

No. of focus	*Age yrs.*	*Sex*	*Duration before opn.*	*Abscess*	*Sinus*	*Anti-biotic group*	*Anti-biotic used*	*Days before opn.*	*Locally*	*Days after opn.*	*Type of opn.*	*Diag. confirmed by*	*Healing time of wound*	*Time of immobili-sation*	*Follow-up*	*Result*
18	50	M	12 yrs.	Yes	No	I	Strept. PAS	30	Yes	60	Laminectomy	Hist.	10 dys.	3 mths.	3 yrs. 1 mth.	Very good
19	45	F	6 mths.	Yes	No	I	Strept. PAS	30	Yes	60	Costo-transversec-tomy D6, 7	Cult.	12 dys.	15 mths.	4 yrs. 6 mths.	Good
20	22	F	3 yrs.	No	No	I	Strept. PAS	90	Yes	7	Curettage and fusion S.I. bone chips	Cult.	13 dys.	8 mths.	3 yrs. 3 mths.	Very good
21	33	M	8 yrs.	No	Yes	I	Strept. PAS	7	No	77	Ditto	Clin.	12 dys.	2 mths.	3 yrs. 2 mths.	Good
22	17	M	2 yrs.	No	No	I	Strept. PAS	90	No	60	Curettage and arthrodes. ank. fib. graft	Hist. Cult. Biop.	21 dys.	6 mths.	5 yrs. 1 mth.	Very good
23	15	M	3½ yrs.	No	No	I	Strept. PAS	90	No	21	Curettage and arthrod. ankle	Biop.	19 dys.	5 mths.	4 yrs. 3 mths.	Very good
24	23	M	3½ yrs.	No	Yes	II	Strept.	6	Yes	14	Curettage sinus ank. arthrodesis	Cult. Biop.	9 dys.	23 dys.	3 yrs. 8 mths.	Good
25	23	M	2 yrs.	No	No	I	Strept. PAS	10	Yes	80	Curettage os calcis	Cult.	20 dys.	3 mths.	3 yrs. 3 mths.	Good
26	4	M	22 mths.	No	No	I	Strept. PAS (Tb. meningitis 1 yr. ago)	6	Yes	60	Curettage ankle with arthrodesis bone chips	Hist.	30 dys.	29 mths.	4 yrs. 4 mths.	Good
27	37	M	9 yrs.	Yes	Yes	I	Strept. PAS	24	Yes	32	Curettage sh. arthrod.	Cult.	6 mths.	6 mths.	4 yrs. 6 mths.	Good
28	21	F	2 yrs.	No	No	II	Strept. PAS	8	No	22	Curettage sh. and arthrod.	Hist.	13 dys.	4 mths.		Very good

SECTION II

Tuberculous Focus affecting Soft Tissues, involving or not the Adjacent Bone

Group A.—Excision of the Soft Tissues only

No. of focus	*Age yrs.*	*Sex*	*Duration before opn.*	*Abscess*	*Sinus*	*Anti-biotic group*	*Anti-biotic used*	*Days before opn.*	*Locally*	*Days after opn.*	*Type of opn.*	*Diag. confirmed by*	*Healing time of wound*	*Time of immobili-sation*	*Follow-up*	*Result*
29	42	F	14 mths.	No	No	I	Strept. PAS	No	No	90	Partial synovecy.	Hist. Cult.	10 dys.	32 dys.	1 yr. 6 mths.	Poor
30	59	F	6 mths.	Yes	No	II	Strept. PAS	No	No	20	Excision soft tis. knee	Cult.	8 mths.	5 mths.	3 yrs.	Good
31	25	M	1 mth.	Yes	No	II	Strept. PAS	No	No	15	Excision troch. bursa	Hist. Cult.	10 dys.	2 mths.	2 yrs. 6 mths.	Good
32	31	F	13 yrs.	Yes	No	I	Strept. PAS	10	Yes	80	Ditto	Hist. Cult.	10 dys.	10 dys.	2 yrs. 3 mths.	Good
33	9	F	4½ yrs.	Yes	No	I	Strept. PAS	13	Yes	77	Excision abs. lt. hip	Hist.	23 dys.	3 yrs.	5 yrs. 1 mth.	Good
34	9	F	4½ yrs.	Yes	No	I	Strept. PAS	13	Yes	77	Excision abs. rt. hip	Cult.	30 dys.	3 yrs.	5 yrs. 7 mths.	Good
35	58	F	20 yrs.	Yes	No	I	Strept. INH	4	No	86	Ditto	Cult. Hist.	10 dys.	1 mth.	1 yr. 6 mths.	Very good
36	37	M	3 yrs.	Yes	No	I	Strept. INH	30	Yes	60	Excision sub-delt.	Cult. Hist.	14 dys.	44 dys.	1 yr. 6 mths.	Very good
37	28	M	3 yrs.	No	No	I	Strept. PAS	90	Yes	90	Synovestomy wrist	Hist.	12 dys.	2 mths.	2 yrs. 5 mths.	Very good

SECTION II

Group B.—Excision or Curettage of the Trocanteric Focus only

No. of focus	*Age yrs.*	*Sex*	*Duration before opn.*	*Abscess*	*Sinus*	*Anti-biotic group*	*Anti-biotic used*	*Days before opn.*	*Locally*	*Days after opn.*	*Type of opn.*	*Diag. confirmed by*	*Healing time of wound*	*Time of immobili-sation*	*Follow-up*	*Result*
38	29	F	25 yrs.	Yes	Yes	I	Strept. PAS	5	No	42	Curettage gt. troch.	Hist.			2 yrs. 2 mths.	Poor
39	52	F	32 yrs.	Yes	Yes	I	Strept. PAS	30	Yes	36	Curettage gt. troch.	Hist. Cult.	10 dys.			Died
40	44	F	27 yrs.	Yes	Yes	I	Strept. PAS	35	Yes	90	Curettage gt. troch.	Hist.	30 dys.	30 dys.	3 yrs. 3 mths.	Very good
41	31	M	8 yrs.	Yes	No	II	Strept. PAS	No	Yes	30	Curettage gt. troch.	Cult.	30 dys.		4 yrs. 3 mths.	Poor
42	57	F	28 yrs.	No	Yes	II	Strept. PAS	No	No	30	Curettage gt. troch.	Hist.	10 dys.	2 mths.	1 yr.	Good

SECTION III

EXCISION OR CURETTAGE WITHOUT ANTIBIOTIC COVER AT TIME OF OPERATION

No. of focus	*Age yrs.*	*Sex*	*Duration before opn.*	*Abscess*	*Sinus*	*Anti-biotic group*	*Anti-biotic used*	*Days before opn.*	*Locally*	*Days after opn.*	*Type of opn.*	*Diag. confirmed by*	*Healing time of wound*	*Time of immobili-sation*	*Follow-up*	*Result*
1	46	F	3 yrs. 7 mths.	Yes	No	No antibiotics given					Curettage of pubis Bone chips	Hist. Cult.	8 dys.	3 mths.	11 mths.	Poor
2	44	F	20 yrs.	Yes	No	No antibiotics given					Costo-trans-versectomy	Clin. Radiol.		4 mths.	5 yrs. 10 mths.	Poor
3	48	M	3 yrs.	No	Yes	No antibiotics given					Curettage shoulder	Clin. Radiol.	8 dys.	12 dys.	1 yr. 8 mths.	Good
4	13	M	6 yrs.	No	No	No antibiotics. Thought to be rheumatoid arthritis					Partial synovecy	Cult.	10 dys.	7 mths.	2 yrs. 1 mth.	Good

LYMPHANGITIS CARCINOMATOSA

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Secondary malignant disease of the lungs is well recognised in the form of more or less circumscribed, scattered deposits; these metastases, as Mendeloff (1945) emphasised, occur as nodular, solid or linear masses without constant relationship to lymphatics or arterioles; in such cases pulmonary symptoms are usually absent or are not a prominent feature of the clinical picture. Less well known is a second variety of metastatic lesion, first described by Andral (1829) and later by Virchow (1855), in which the tumour cells are found permeating the pulmonary lymphatics, and often in addition the arterioles and small arteries, producing obliterative changes, and even a diffuse pulmonary fibrosis. Full descriptions of the morbid anatomy and histology of the pulmonary condition were subsequently given by Troisier (1873) and Raynaud (1874).

Although several American, French and German reports have appeared emphasising the presenting feature of severe, unrelieved and progressive dyspnœa, only 37 cases have been described in the few (eight) British reports (Bristowe, 1868; Bennett, 1871; Lorain Smith, 1909; Wu, 1936; Lister, 1949; Morgan, 1949; Harold, 1952; Chandler and Telling, 1952). Harold (1952) discovered 13 cases among 836 consecutive necropsies involving 170 cases of malignant disease and suggested that the condition occurred more frequently than generally supposed.

This paper describes four more cases and discusses the symptomatology, the radiological and pathological features, and the pathogenesis.

Case 1. A 51-year-old woman, on whom a right mastectomy had been performed in 1944, was admitted on September 21, 1951, complaining of the onset over a few days, two months previously, of persistent dyspnœa and cough with some sputum. Her appetite decreased, with some loss of weight. A few days before admission she developed pain across the upper chest. She was obese and plethoric, dyspnœic at rest and slightly cyanosed. Some impairment of the percussion note was noted at the right lung base. Showers of crepitations and some rhonchi were heard over the right lung and scattered moist râles over the left lung. Radiographs of the chest showed increased density of lung markings radiating from the hilum on each side with patchy consolidation centrally on the right side.

Her condition deteriorated; she became very cyanosed, grossly dyspnœic and orthopnœic. The lungs showed signs of basal consolidation, and death occurred on October 10, 1951.

Necropsy Findings. The pleural cavities contained small quantities of fluid. The lungs were congested and œdematous. Universal subpleural yellow

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streaking was visible over both lungs, suggesting neoplastic infiltration of lymphatic vessels; there were no large secondary deposits. The lymph nodes of the internal mammary and the para-aortic chains were infiltrated.

Histology. Sections of a mediastinal lymph node confirmed the presence of deposits of a cuboidal-celled carcinoma grouped in acinar formation. Less differentiated deposits were observed in large numbers of the pulmonary lymphatic vessels. No cancer cells were visible in the lumen of the blood vessels, but there was some evidence of intimal thickening. The alveoli contained no neoplastic cells, but many of their walls were lined by a homogeneous, eosinophilic structureless material—apparently fibrin. (See Fig. 1.)

CASE 2. A 42-year-old woman, on furlough from India, was admitted on September 1 complaining of pain, of three days' duration, situated in the left side of the chest postero-laterally and worse on breathing. Cough apparently had been present for about two weeks with slight sputum, occasionally brown or blood-stained. She was not cyanotic or dyspnœic. There was deficient air entry at the left lung base, with a friction rub and some scattered crepitations. A small irregular mass was palpable in the right iliac fossa. The temperature was 99·6°. Chest radiographs showed some accentuation of the lung markings; superimposed on these linear streakings there were very slight degrees of soft mottling in the right lower and reticulation in the left lower lung fields.

She had previously been referred to the Out-Patient department on August 29, 1952, complaining of central colicky abdominal pain. This had first occurred one evening about two weeks before with eventual relief in the morning with vomiting and then recurred one week later; subsequently there was intermittent colicky pain almost every day about four hours after meals, with diminution in appetite and slight constipation. Examination at that time had revealed no abnormalities except a hard lump palpable *per rectum* high up in the pouch of Douglas. She had suffered from occasional attacks of malaria in India, where an appendicectomy was said to have been performed in 1951.

For some days after admission she passed several fluid motions daily. Gradually there developed some cyanosis and slight dyspnœa on effort. On September 6 she awoke definitely cyanosed, dyspnœic and orthopnœic. The left basal pleural rub was still present, with only a few scattered adventitial sounds in both lungs and slight diminution of breath sounds in the right lower lobe. The blood pressure had fallen from 135/70 on admission to 110/60, the pulse rate was 120 per minute and the respirations were 32. Dyspnœa increased —culminating eventually in great inspiratory indrawing of the supraclavicular fossæ and the epigastrium. Death occurred on September 11, 1952.

Necropsy Findings. A left ovarian carcinoma had extended into surrounding tissues and structures. The pleura of the left lung, particularly at the base, showed some dry fibrinous exudate. Multiple subpleural white nodules, rather larger than pinhead size, were scattered over the surfaces of both lungs—clearly malignant deposits in the lymphatics. The lungs were heavy and moderately œdematous; on slicing, more small nodules of new growth were visible. The cut orifices of the small bronchi were rendered prominent by malignant deposits around the walls.

Histology. Sections confirmed the widespread presence of a columnar-celled adenocarcinoma originating in the ovary. The lungs showed neoplastic tissue widespread in the lymphatics. Several blood vessels showed tumour-cell emboli; many showed partly organised thrombi invaded by cancer cells. Intimal thickening was practically absent. There was little vascular change

even in the presence of large perivascular lymphatic deposits. There appeared to be invasion of the bronchial walls in parts and cancer cells were found in many alveoli. (See Fig. 2.)

CASE 3. A 73-year-old man attended the surgical out-patient clinic on June 23, 1952, complaining of low epigastric pain, of six weeks' duration, unrelated to meals and present throughout the day though worse at night, and also weakness, constant nausea and occasional vomiting. His general condition was good for his age; the epigastrium showed some distension, and a mass and splash were detected. When admitted on July 13 his general condition was extremely poor, with jaundice and marked distension of the abdomen, which contained a hard mass filling the right and extending into the left upper quadrant. Death occurred on July 14.

Necropsy Findings. A massive growth originating in the pancreas had spread outwards into neighbouring organs.

Small pleural effusions were present bilaterally. The trachea contained blood-stained froth. Both lungs showed multiple miliary nodules of new growth scattered throughout. Petechial hæmorrhages were present on the surface of the base of the left lung. Invaded and enlarged lymph nodes were present in groups below the bifurcation of the trachea and also paratracheally, extending up to the larynx.

Histology. A section from the pancreatic carcinoma showed a solid anaplastic mass of cells with little supporting tissue. In the lungs, spread of the growth had occurred in the pulmonary lymphatics and in some smaller branches of the pulmonary artery, with occasional intimal thickening. Some of the alveoli contained cancer cells. (See Fig. 3.)

CASE 4. A 67-year-old man was admitted to hospital on January 27, 1949, having passed no urine during the previous twenty-four hours. He had suffered for some time from increased frequency of micturition, greatly aggravated nocturnally in the preceding six weeks. He was obese but not dyspnœic, with a sallow complexion and œdema of the lower eyelids. The bladder was not distended. The prostate felt very hard and enlarged. Catheterisation produced only a few millilitres of blood-stained urine. Cystoscopic examination suggested a carcinoma of the prostate infiltrating around the ureters. A de Pezzer catheter was inserted. Subsequently he developed extensive ecchymoses of the penis and scrotum and hæmorrhagic discolouration of the skin of the right groin, flank and thigh, lower abdominal wall and both arms. Blood count showed Hb. 64 per cent., W.B.C. 15,000 per c.mm. and platelets 180,000 per c.mm. Bleeding time was 8½ minutes and clotting time 9 minutes. The blood urea nitrogen rose from 98 mg. per 100 ml. on admission to 154 mg. by February 2. His condition deteriorated. The anuria persisted. Death occurred on February 3, 1949.

Necropsy Findings. The prostate showed a primary carcinoma involving the left lateral and middle lobes with extension into the bladder. There was widespread neoplastic invasion of numerous lymph nodes, pelvic, abdominal, thoracic and supraclavicular. The pleural surfaces of both lungs showed an unusually well-defined network of cancerously infiltrated lymphatics. On slicing the lungs were œdematous but showed no evidence of blood-borne deposits. Histological sections are no longer available. (See Fig. 4.)

FIG. 1.—Case 1. Chest radiograph of 8.10.51.

FIG. 2.—Case 2. Chest radiograph of 9.9.52.

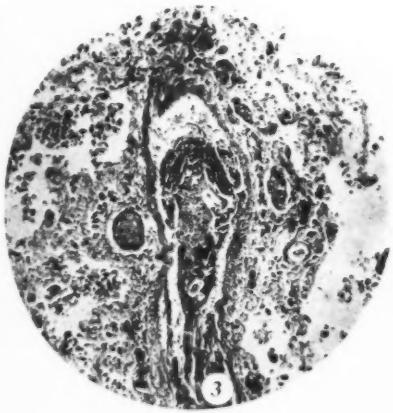

FIG. 3.—Case 2. Lung showing blood vessel filled with thrombus with central invasion by cancer cells at one end of the cut vessel and permeation of the perivascular lymphatics and some alveoli. ×85.

FIG. 4.—Case 3. Lung showing blood vessel containing cancer cells and red blood cells and cancer cell permeation of the perivascular lymphatics. ×85.

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Discussion

The outstanding feature in most cases of this condition is the marked disproportion between the severe respiratory symptoms and the minimal physical signs. The most frequent manifestations are dyspnœa with tachypnœa, cough with slight sputum, cyanosis and general physical deterioration; of this tetrad dyspnœa is a cardinal presentation. Mendeloff (1945) described it as severe, unremitting and progressive, and characterised by a gasping tachypnœa, while Boccard (1925) referred to " la forme asphyxiante aigüe de la carcinose secondaire du poumon." Occasionally the dyspnœa has been paroxysmal, prolonged or wheezing and mistaken for asthma, though without the characteristic response to antispasmodics. In some cases there has been slight blood streaking of the sputum. Hæmoptysis may occur in cases secondary to bronchial neoplasm (Harold, 1952). Mendeloff (1945) noted chest pain, characteristically pleuritic in nature, in 10 per cent. of cases. Brill and Robertson (1937) described a clinical picture, predominantly that of right-sided heart strain and failure, characterised by rapid development over a period of three to eight weeks without previous evidence of cardio-vascular or pulmonary disease. Despite the widespread nature of the metastases the paucity of physical signs has been emphasised in all reports. This might be expected in view of the rarity of involvement of the alveoli in the process. No abnormal signs may be detected in the lungs (Harold, 1952). However, the most frequent findings are diminution of breath sounds and the presence of sibilant rhonchi or moist râles (Wu, 1936). Expiratory wheezing and pleural friction may occasionally be heard. Signs of consolidation, or collapse, are rare. The presence of pleural effusion may in some cases be indicative of subacute cor pulmonale. Low-grade fever may be present. Right ventricular enlargement may be found, the electrocardiogram showing evidence of right axis deviation or cor pulmonale. This may occur even in the absence of widespread pulmonary arteriolar obliterative changes (Wu, 1936).

This pulmonary neoplastic condition usually arises insidiously, but may be precipitated by an acute respiratory irritation or infection. Perusal of the literature reveals the following possible presentations:

(1) *With respiro-cardiac features*, consisting of

(*a*) severe unrelieved dyspnœa and some or all of the other components of the tetrad—as in most cases;

(*b*) paroxysmal dyspnœa or prolonged asthmatic attack (Mendeloff, 1945; Mueller and Sniffen, 1945, case 1, and Harold, 1952);

(*c*) apparent respiratory tract infection, mainly cough, sputum and malaise, etc. (Mueller and Sniffen, 1945, cases 4 and 5; Hauser and Steer, 1951, case 3), even to the misdiagnosis of tuberculosis (O'Brien, 1947); or

(*d*) right heart failure, the subacute cor pulmonale of Brill and Robertson (1937) (Krutzsch, 1920; Greenspan, 1934; Krygier and Brill, 1942),

occurring in patients who have—

(i) a previous history of neoplastic disease;

(ii) other symptoms and signs which may or may not suggest

new growth; or

(iii) no other symptoms and signs—*i.e.*, a silent primary growth, as emphasised by Schattenberg and Ryan (1941), Lister (1949), Morgan (1949), Harold (1952), and others.

(2) *Without respiro-cardiac features* and therefore found incidentally in patients—

(i) with an illness definitely neoplastic in nature (Mueller and Sniffen, 1945, cases 9 and 1; Minor, 1950; Harold, 1952);

(ii) with no such unequivocal evidence of malignancy (Moon, 1929; Stebbins and Carns, 1935; Wu, 1936, cases 1 and 2); or

(iii) with a silent neoplasm or death from other causes.

Hauser and Steer (1951) have stressed the importance of the silent primary growth and also the masking of the primary neoplastic symptoms by the pulmonary symptoms.

The average age at onset was found by Poppi (1935) to be 42·6 years, but in cases showing metastases from gastric carcinoma the age was 38 years. Wu (1936) found that 20 of 54 cases were under 40 and 36 under 50. The age limits extend from 15 (Bennett 1879) to 77 (Wu, 1936). The slight preponderance of males may be attributed to the greater frequency of gastric neoplasms in men.

Pulmonary symptoms were shown by two of the cases described above—females aged 53 and 42 years; the former had a previous neoplastic history, while the latter had symptoms not initially attributed to a new growth. The third and fourth cases—males aged 73 and 67 years—showed no disproportionate dyspnœa; the symptoms were neoplastic.

Radiological Appearances

The first detailed radiological accounts were given by Lorenz (1921) and Assmann (1924). The latter referred to the spreading, branching string-pattern radiating from the enlarged hilar shadows to the periphery. Mueller and Sniffen (1945) described a "fine miliary nodular and linear process involving both lungs in an uneven design of trabeculation." The radiological picture consists of one or more of the following features: (1) enlarged hilar shadows, (2) trabeculation or reticulation, or a string network in which however only (3) the miliary mottling or (4) the linear streaking may be visible, and (5) secondary features such as pleural effusions, collapse or consolidation, and sometimes (6) right heart enlargement. These appearances are more marked in the central and basal portions of the lung fields, and occasionally may be more evident on one side or even unilateral. Rarely, suggestive radiographic appearances have been observed several weeks before the onset of dyspnœa (Mueller and Sniffen, 1945; Harold, 1952). Apparently normal lung fields with portable radiography were noted by Harold (1952) in one case persisting to death.

Mueller and Sniffen (1945) considered that the radiological findings were explained entirely by the lymphatic invasions and maintained that vascular congestion and damage, bronchial infiltration, pulmonary œdema and fibrosis were not found to the extent that would produce visible changes in the

radiograph; the occasional infiltration of the alveolar spaces by neoplastic cells might account for the larger densities sometimes observed.

Morbid Anatomy and Histology

Almost any organ may be the source of the primary neoplasm; however in more than half to three-quarters of all cases the primary growth is in the stomach. Less frequently the bronchus, breast, pancreas and prostate are involved. The primary sites in the four cases here described were the breast, ovary, pancreas and prostate respectively. Only one other report (Moretti, 1933) has described the primary growth in the ovary. Wu (1936) attached no special importance to the structural type of the primary tumour. Mueller and Sniffen (1945) noted that in nine of their ten cases the primary neoplasms were undifferentiated.

The gross pathological appearance in the lungs, according to Schattenberg and Ryan (1941), are usually characteristic if sufficiently marked. The lung is larger, firmer and more moist than normal. There is a dilatation of the pleural lymphatic channels which causes them to stand out prominently and the lobules of the lung are delineated. At the points of intersection of the lymphatics small yellowish-white nodules may be seen. On slicing, the lung appears mottled and involvement of the peribronchial and perivascular lymphatics is evident. Small plugs can be expressed sometimes from these involved vessels.

Microscopically the lymphatic vessels, less often the arterioles and in some cases the bronchial walls and the alveoli show changes. Tumour cells are found filling the perivascular, peribronchial, pleural and interlobular-septal lymphatics. Compression of arterioles and veins by the surrounding dilated lymph vessels may occur. Mueller and Sniffen (1945) and Mendeloff (1945) reported invasion of the bronchial walls and the bronchial mucosa. They and Hauser and Steer (1951) also noted a few tumour cells scattered in alveoli.

Morgan (1949) found evidence of pulmonary vascular changes in about one-third of the reported cases. Tumour emboli in the pulmonary arterioles were first recognised in 1903 by Schmidt, and even earlier, endarteritic thickening was reported in 1889 by Girode, who apparently regarded it as an incidental finding. Mueller and Sniffen (1945) clearly described the tumour-cell emboli widespread in the arterial system, usually associated with thrombotic material (though thrombosis apparently might occur alone) and resulting in various degrees of vascular occlusion and organisation, the thickening of the intima of the small arteries and arterioles by acellular fibrous tissue with widely separated fibres, presumably due to fluid, the intense adventitial fibroblastic reaction apparently caused by cancer cells in the perivascular lymphatics, the occasional tumour-cells in the media and intima (sometimes accompanied by lymphocytic infiltration) and at times in the alveolar capillaries. The veins were free from changes, except occasionally cancer-cell invasion of the outer layers of the wall and fibrous intimal thickening.

Hypertrophy of the right side of the heart was found by Wu (1936) in 11 of 49 cases, of which 5 showed obliterative vascular changes. Of the 11 cases tabulated by Morgan (1949) " intravascular fibrosis " (which comprises fibrous organisation of thrombi and endarteritis) was present in 8 and

cancer-cell emboli and recent thrombosis in 2 more.

The six cases of Hauser and Steer (1951) showed fibrosing perivascular, vascular and pulmonary changes associated with the lymphangitic carcinomatosis.

Pathogenesis

The mode of spread to the lungs has been discussed by several authors. Girode (1889) described three possibilities: (1) hæmatogenous extension via the veins and right heart to the pulmonary arterioles with subsequent invasion of the lymphatics; (2) direct lymphatic extension through the diaphragm with invasion of the pleural and pulmonary lymph vessels; (3) lymphogenous extension via the thoracic duct to the hilar lymph nodes with retrograde invasion of the pulmonary and pleural lymphatics. As regards the latter it should be noted that chylous ascites has been reported only twice (Gamberini, 1928; and Poppi, 1935).

Hauser and Steer (1951) suggested the importance of spread along the paraœsophageal lymphatics and thence through the hilar anastomoses into the lung parenchyma. Willis (1952) considered that the hilar glands were involved via the cœliac and posterior mediastinal groups, which invariably contained tumour deposits. Von Meyenburg's (1919) concept—the most generally accepted—involved spread of the tumour cells from the stomach to the perigastric lymph nodes and next to the tracheal and mediastinal groups with lymphatic stasis and retrograde dissemination in the lungs from the hilum. The importance of hilar involvement was stressed by Wu (1936), who noted that visible cancer invasion had occurred in 33 of 35 cases where the condition of the mediastinal and hilar lymph nodes was mentioned. On the other hand, in chest radiographs of patients with extensive abdominal neoplasm Johnstone (1954) has sometimes observed evidence of secondary deposits on the pulmonary aspect of the diaphragm.

Morgan (1949) opposed the theory of retrograde lymphatic spread. He suggested that small tumour emboli in the pulmonary circulation (reached either directly via the thoracic duct and the superior vena cava, or indirectly via the hepatic veins and the inferior vena cava) might become arrested in the smaller arterioles with subsequent spread proximally and distally along the various vessels, resulting in thrombosis, intravascular fibrosis and access to the pulmonary lymphatic system with final involvement of the hilar lymph nodes. He believed that the appearances in his case suggested continuity between cancerous emboli in the blood vessels and tumour cells in the lymphatics, and indeed such continuity had been traced in one of Schmidt's (1903) cases. Schierge (1922) considered it possible for the cancer-cell emboli to pass through the pulmonary capillaries into the lymphatics without being arrested.

It is quite possible that both lymphatic and vascular spread take place. It is of interest here that Hauser and Steer (1951) described a case in a male who had undergone a left thoracoplasty for tuberculosis, in which the right lung showed generalised extensive lymphangitis carcinomatosa, while the compressed left lung contained no tumour. Further, many cases with a clinical presentation similar to lymphangitis carcinomatosa have shown only vascular dissemination in the lungs (Mason, 1940; Schmidt, 1903, discussed by Brill and Robertson, 1937; Morgan, 1949, reference to 9 cases). It might be more

appropriate, therefore, to refer to "diffuse pulmonary lympho-vascular carcinomatosis."

The importance of cancer-cell emboli in the causation of the obliterative vascular changes has been recognised. Morgan (1949) found such emboli present in 24 of 30 cases showing obliterative changes. Wu (1936) described a gradual deposition of platelets in and around the emboli with the production of thrombosis and later organisation. The intimal thickening, or endarteritis, he thought, might be due either to thrombotic blockage of the lumen elsewhere in the affected vessel with reduced blood flow, or to a direct toxic effect of the cancer cells. Von Meyenburg (1919) regarded the presence of cancer cells in the blood vessels as a secondary feature due to invasion of the walls from the perivascular lymphatics. Both he and Greenspan (1934) considered the obliterative endarteritis an intimal reaction to the perivascular lymphatic deposits. Greenspan (1934), however, observed the typical obliterative intimal changes regularly present in arterioles which contained cancerous emboli and were surrounded by lymphatic metastases. The œdematous thickening of the arterioles, especially the intima, Wu thought to be a local manifestation of the general interstitial œdema of the lung following lymphatic obstruction. Brill and Robertson (1937), who apparently did not appreciate the importance of the tumour-cell emboli, attributed the arteriolar changes to (i) pressure effect from the adjacent cancer-laden lymphatics, (ii) connective-tissue proliferation due to the desmoplastic nature of the growth, and (iii) direct contact invasion of the walls of the vessels. Mueller and Sniffen (1945) believed that cancer-cell emboli were the sole cause of the occlusion of the arteries, since thrombosis was absent in the veins, and that the intimal thickening was not a local manifestation of pulmonary œdema (the veins not being involved) but was associated with a combination of intravascular thrombosis and invasion of the vessel wall.

The hypertrophy of the right side of the heart is generally considered to be due to the arteriolar blockage, but in view of the experimental work of Fineberg and Wiggers (1936) it must be allowed that arterial compression by the distended perivascular lymphatics might play a part, as has been suggested by Goldmann (1931).

Such compression may be a factor in the causation of the characteristic dyspnœa. Mendeloff (1945) considered the respiratory difficulty to be the resultant of three main factors: (*a*) the neoplastic permeation of the perivascular and peribronchial lymphatics interfering with the normal gaseous diffusion across the pulmonary epithelium; (*b*) the inflammatory response around the invading cells producing at first interstitial œdema and hyperæmia and after a period of time a stiffening and inflexibility of both conducting and respiratory portions of the lungs; and (*c*) the probable impairment of the structural and functional integrity of the bronchial musculature through the adjacency and frequent invasive activity of the neoplastic cells. The effect of these factors would be to promote stimulation of the Hering-Breuer reflex with resulting inhibitory effects on a respiratory centre concomitantly affected by anoxia. Other possibilities in the pathogenesis of the respiratory embarrassment have been suggested—œdema of the lungs (Girode, 1889); narrowing of the bronchioles and reduction of the respiratory surface (Bard, 1906);

a cardiac element (von Meyenburg, 1919); and a toxic action on the respiratory centre by neoplastic products (Goldmann, 1931).

Wu (1936) has referred to the possibility of a biological peculiarity of the tumour and a special anatomical constitution of the patient working together in the production of the pulmonary condition. Jarcho (1936) attempted, with considerable success, to show that lymphangitic carcinomatosis of the lungs was merely the pulmonary manifestation of a distinctive variety of carcinoma metastases, which also tended to produce characteristic hæmatological changes, such as a hæmorrhagic diathesis, anæmia or leucoerythroblastosis through involvement of the bone marrow, and might in occasional cases be associated with diffuse carcinomatous infiltration of the ovary producing the Krukenberg tumour—" a diffusely infiltrative carcinoma."

Differential Diagnosis

The differential diagnosis has been discussed by Mueller and Sniffen (1945). Clinically and radiologically there may be a strong resemblance to miliary tuberculosis, though this usually occurs in a younger age group. Radiologically the hilar shadows are less dense and less enlarged; elsewhere fine nodular shadows are typically found. In pulmonary congestion and œdema the lung fields are often hazy and the blood vessel shadows tend to become smaller towards the periphery. Pneumoconiosis usually presents much denser and more circumscribed nodular opacities. In sarcoidosis the hilar lymph node involvement is usually characterised by sharply defined bilateral masses; the pulmonary clinical manifestations are usually minimal and other evidences of sarcoidosis may be present. In both fibrosis with emphysema and bronchiectasis when radiographic similarity is present there is usually a much longer and different clinical history. Any radiographic similarity in some cases of resolving atypical pneumonia is discounted by the definite preceding respiratory infection, absence of dyspnœa and cyanosis, and, in about half of the cases, the presence of cold hæmagglutinins and agglutinins for streptococcus M.G. in the serum.

The important features are therefore severe dyspnœa disproportionate to the minimal physical signs, a heart of normal size or with evidence of right-sided enlargement in the absence of mitral stenosis, chronic bronchitis with emphysema or pulmonary stenosis, the absence of signs of congestive cardiac failure or of renal disease, the presence of the characteristic radiological picture and the failure to respond to any therapy. It is essential to be aware of the different modes of presentation, to consider it as a possible cause of severe dyspnœa, and to look for its presence in cases suggesting an underlying neoplastic condition.

Summary

1. Four cases of lymphangitis carcinomatosa, in two females aged 53 and 42 and two males aged 73 and 67, following primary neoplasms of the breast, ovary, pancreas and prostate respectively, are reported.

2. The possible modes of presentation of the condition are described—inconspicuous thoracic signs in the presence or absence of certain respiro-cardiac symptoms occurring in overt or latent neoplastic conditions.

3. The clinical, radiological and pathological features and the pathogenesis are discussed.

4. The more frequent recognition of lymphangitis carcinomatosa can be seen to depend on awareness of it as a possible cause of severe dyspnœa, and searching for evidence of its presence in any case of possible neoplastic disease.

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THE CHANGING PLACE OF ARTIFICIAL PNEUMOTHORAX IN THE TREATMENT OF PULMONARY TUBERCULOSIS

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Since the comparatively recent introduction of chemotherapy and resectional surgery in the treatment of pulmonary tuberculosis, artificial pneumothorax (A.P.) has suffered a partial eclipse. It is perhaps too early to say with any certainty what place, if any, it is to have in the future. Nevertheless, we have felt that it would be of interest to review the results of A.P. treatment carried out at the East Ham Chest Clinic and Plaistow Hospital Chest Unit since 1942, to describe our experience in relation to certain aspects about which there is no unanimity, and to evaluate the method in the light of modern advances in treatment.

Even before the advent of chemotherapy the limitations, difficulties and disappointments of A.P. treatment had been increasingly recognised (Ellman, 1949), and more discrimination was being displayed in its application. The most important effect of prolonged chemotherapy has been in assisting the conversion to quiescence of a much greater proportion of patients, without the need for active intervention. This, however, has been to some extent overshadowed by the widened scope and increased effectiveness of thoracic surgery, especially in the field of resection; the full effect of chemotherapy upon A.P. treatment has yet to be established. It is apparent, however, that more patients are rendered suitable for A.P., often in a shorter time, and that there is a reduction of the incidence and importance of serious complications, such as spread of disease or empyema.

Snell (1953) pointed out that no case of empyema complicating A.P. treatment had occurred at Colindale or Baguley Hospitals since 1947. This was presumably by reason of more careful selection and management of cases combined with the discriminate use of chemotherapy.

The present is a transitional period during which widely divergent views on treatment are held. In Holland, A.P. treatment has been virtually abandoned in favour of treatment by prolonged bed rest, chemotherapy and subsequent resection if conservative and chemotherapeutic measures fail. Keers (1953) endorses this attitude, and a similar trend has been noted in Liverpool and elsewhere. Toussaint (1955) feels that most cases can be effectively treated by intensive medical treatment aided by chemotherapy, and recommends artificial pneumothorax therapy as an additional safeguard for a short period during rehabilitation.

Ellman (1949) concluded that pneumothorax, discriminately used, could

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achieve satisfactory end results and survival rates. Simmonds *et al.* (1952) felt that, although A.P. properly applied and managed could still give good results, we were getting to the point where, in our efforts to avoid any complications, we were unlikely to venture on an A.P. at all. Snell (1953) held firmly that there was still a very definite place for this treatment. Reviewing the treatment of tuberculosis, Amberson (1955) observed that A.P. was employed much less often since chemotherapy became available, largely because of the necessarily long duration of the treatment and the incidence of pleural complications.

In making any assessment it should be recognised that pulmonary tuberculosis is a generalised disease with local manifestations in the lungs and a tendency towards natural resolution under favourable conditions (Ellman, 1939; Toussaint, 1955). Moreover, no single method of treatment is likely to prove effective in every case. Further, the environmental and social conditions, no less than the clinical condition, must be considered when deciding about each individual case.

Accepted Facts regarding A.P. Treatment

There is general agreement regarding the superiority of A.P. treatment in suitable cases over rest alone. (Shaw, 1933; Hartley, Wingfield and Burrows, 1935; Bentley, 1936; Foster-Carter *et al.*, 1952). In the light of experience certain indications and contraindications for A.P. treatment have been established, but the former are now controversial, while the latter are more precise.

An A.P. should not be attempted in the presence of endobronchial disease, recent exudative disease, nor in the presence of fibroid or fibrocavernous lesions. An adequate period of preliminary rest in bed is essential, although with chemotherapy this period can be shortened considerably and many cases which would otherwise have been considered unsuitable for A.P. treatment may be made suitable. The dangers of a "crash" pneumothorax are well known and need no emphasis.

Foster-Carter *et al.* (1952) have shown that the mere presence of adhesions did not affect the prognosis or the incidence of pleural complications, provided cavity closure was achieved; patients with persistently open cavities showed a high incidence of empyema and a high mortality. Similar findings have been reported by Bignall (1950) and Sadler (1954). The underlying factors would appear to be tuberculous endobronchitis or intrapleural rupture of a cavity; in all cases reported by Farquharson (1951) in which empyema was associated with atelectasis, the whole lung was collapsed, suggesting that the latter had occurred. The danger of persistent cavitation within a major atelectasis in an A.P. case was recognised by Houghton (1950) and Cuthbert (1950) and nobody now would persist with an A.P. that presents these features.

The importance of having uniform skilled control of an A.P. has been stressed by Young (1949), Scadding *et al.* (1951), Harris *et al.* (1952) and Livingstone (1955). Special hazards in this respect are empyema, spontaneous pneumothorax, hæmothorax, air embolism and possible premature loss of the A.P.

Factors regarding which there is no General Agreement

Indications for inducing A.P. were fairly wide until the advent of antibiotics. Since then, with the advance of resectional surgery, together with the recognition of the dangers and complications of A.P. treatment, opinion has swung in the reverse direction.

In the past opinions have differed as to the optimum time for terminating an A.P., but the modern tendency is towards earlier discontinuance.

It will be some time before any assessment can be made of the effects of treatment with A.P. and chemotherapy combined, and it may well be that a shorter period of collapse will prove adequate.

The reason why effusions occur with some A.P.s but not with others is still not clear, nor why some effusions become purulent. Major endobronchial disease is a potent cause, but there are many cases in which it does not appear to be operative. Although fibrothorax, which often follows empyema and hæmothorax, restricts the lung and predisposes it to infection, no proper investigation has been done to determine to what extent this is so.

Material

The material in this study consists of patients whose A.P.s were commenced after 1.1.42, and who have been managed almost entirely at the East Ham Chest Clinic and Plaistow Hospital Chest Unit under the continuous supervision of one of us (P.E.). All patients whose A.P.s were discontinued less than twelve months after induction, or whose A.P.s are still continuing or have been very recently stopped, have been excluded from the investigation. A further group of patients who had received chemotherapy in conjunction with A.P. induction were also excluded. Refills have been for the most part done by the same personnel throughout.

There remained for assessment 152 patients, of whom 140 (with 162 A.P.s) have been fully followed up; death occurred in 8. Among the 12 patients who were not followed 2 were known to be still alive, 7 were known to be dead and the other 3 who could not be traced have been presumed to be dead, giving a total maximum possible death rate of 18/152 (12 per cent.).

As the results in the cases which had bilateral A.P.s were no different from those with unilateral A.P. they have been grouped together for analysis.

Table 1 (Appendix) shows the distribution of the cases according to age, sex and initial extent of disease. Group 1 cases had only one zone affected, Group II had two or three zones affected, and Group III had four or more zones affected. Thus, Group I cases were all unilateral, Group III were all bilateral and Group II included cases in both categories.

In assessing the material the following criteria were adopted:

1. Quality of Pneumothorax

Good A.P. immediately ..	Selective collapse; no adhesions or atelectasis; early cavity closure.
Good A.P. after adhesiotomy	Ditto.
Fair A.P. after adhesiotomy	Selective collapse with cavity closure but some adhesions still present, insufficient to affect the collapse and/or segmental atelectasis, and/or minimal effusion.
Bad A.P. after adhesiotomy	Significant adhesions present and poor or contraselective collapse, and/or lobar or total atelectasis, and/or persistent cavity, and/or moderate or large effusion.

In the last two groups one or more of the features were considered sufficient to place it in the appropriate category. Those cases with bad A.P.s after adhesiotomy include 8 in which cavity closure was not achieved and their outcome is discussed below.

In the final assessment the condition of the patient as a whole and that of the treated lung have been considered separately.

Final State of Patient

Good	Good general condition and respiratory capacity; symptomless; normal life; working at previous or similar employment.
Fair	Fair general condition and respiratory capacity; some symptoms; modified life; sheltered or part-time employment.
Bad	Confined to bed or up for limited periods; unable to work; symptoms present; poor respiratory capacity.

Final State of Lung

Good	Complete re-expansion; no fluid or pleural thickening; no mediastinal shift; inactive disease; negative sputum.
Bad	Incomplete re-expansion; fluid or pleural thickening of more than moderate extent; mediastinal shift; active disease; sputum positive.
Fair	Cases which do not fall into either of the above groups.
Fibrothorax	Gross contraction of the lung, due to pleural thickening and fibrosis, causing almost an opaque hemithorax and re-retraction of the chest wall.

General Results

Analysis showed that the results regarding the patients were good in 68 per cent., and the results regarding the lungs were good in 51 per cent.; 14 per cent. of the patients did badly, 15 per cent. of lungs were classed as bad finally and 12 per cent. resulted in fibrothoraces. The death rate in this material was 8 out of 140 patients (5·7 per cent.). (See Table I, Appendix.)

In the general assessment of results the following factors were considered:

(*a*) *Age and sex.* These were fairly evenly divided between the groups and did not appear to influence the results.

(*b*) *Initial extent of disease.* The results confirm the findings of previous investigators that the more extensive the initial disease, the less chance of getting a good result.

This generalisation, of course, does not apply to individual cases, some of whom did very well in spite of extensive disease; some others with initial minimal disease did very badly.

(*c*) *Quality of the A.P.* Good A.P.s, either immediately or following adhesion section, were obtained in 69 per cent. of Group I cases, in 67 per cent. of Group II cases and in 77 per cent. of Group III cases. It is thus seen that the initial extent of disease had no influence on the quality of A.P. likely to be obtained.

The results for the patient as a whole and for the lung, when a good A.P. had been obtained, were better than when the A.P. was only fair or bad. Further, though it was not uncommon to get a good result in the patient as a whole when the A.P. had been classed as bad, it was unusual to get a good

result as regards the lung—*i.e.* bad A.P.s—though often finally arresting the disease, commonly affected the function of the lung adversely. (See Tables II and III Appendix.)

It was possible to separate the influence of failure to obtain cavity closure from other causes of bad initial A.P. Thus of the 23 bad A.P.s in all groups 15 were associated with cavity closure and in 8 the cavities remained open. Of the latter 6 patients did badly (5 died) and the results, as far as the lung only was concerned, were bad in 7. On the other hand, of the 15 where cavity closure was achieved only 1 patient did badly and there were no deaths.

(*d*) *Mortality.* Deaths occurred in 1 out of 39 patients in Group I, in 5 out of 79 patients in Group II and in 2 out of 22 patients in Group III.

Only 2 of the patients who died had good A.P.s; 4 had bad A.P.s in spite of adhesion section, and the rest were only fair. Sputum conversion was not achieved in any of the patients who died. In all cases the disease was either bilateral at the outset or became bilateral subsequently, and in 3 cases there were persistent tension cavities (bilateral in 1 case). Serious complications of the A.P. occurred in only 2 instances—hæmothorax occurred in 1 case with a tension cavity, and in the other rupture of a cavity was followed by total atelectasis of the lung and a massive effusion.

(*e*) *Complications.* Complications of the Artificial Pneumothoraces occurred as follows:

36 cases of pleural effusion		27 complicated 9 simple
7 „ „ potential empyema		
58 „ „ atelectasis		51 segmental 5 lobar 2 total lung
7 „ „ tension cavity		
1 „ „ hæmothorax		
1 „ „ spontaneous pneumothorax		

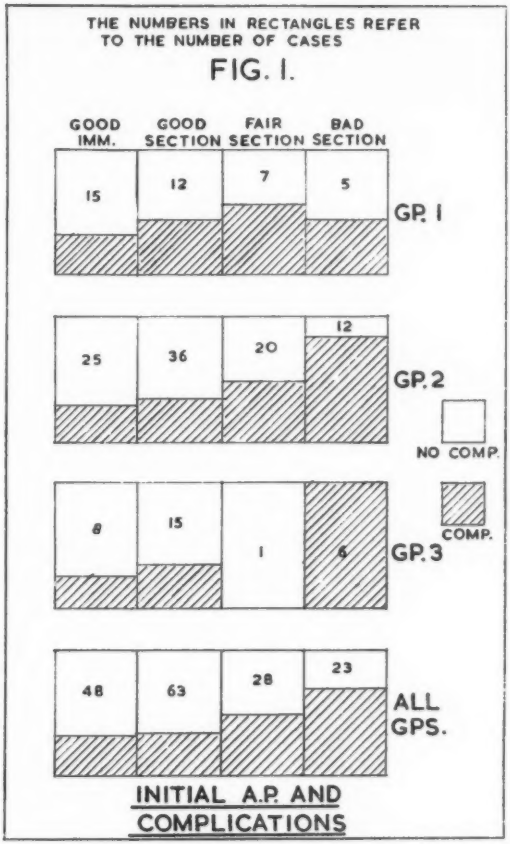
Our figures show, as one would expect, that the incidence of complications was related to the quality of the A.P.—the worse the A.P., the greater the incidence of complications (Fig. 1).

2. Atelectasis

Atelectasis of a lung segment after the induction of an A.P. is a frequent occurrence. This is not surprising, since some degree of bronchial disease is present in most cases as shown by Clegg (1953) and others. As a general rule this is insignificant and does not influence the outcome; re-aeration usually occurs or the segment shrinks to a fibrotic scar.

Houghton (1950) and Maher-Loughnan (1950) regard lobar or total atelectases as potent causes of serious complications such as effusion, empyema or spread of disease. Sadler (1954) agreed that atelectases are related to the incidence of effusion, but showed that the extent of initial disease in the A.P. lung may have been a relevant factor.

Farquharson (1951), Scadding *et al.* (1951) and Foster Carter *et al.* (1952) found that segmental and lobar atelectases were not important and did not influence the mortality rate or the incidence of complications; the majority



of atelectases re-aerated (Scadding *et al.*, Farquharson, Sadler), and only totally atelectatic lungs were associated with spreads or reactivation (Sadler) or with empyema (Farquharson).

Mitchell (1951) found a strong relationship between major atelectases and ultimate fibrothorax, but this may have been a direct result of associated effusions, as shown by Sadler (1954).

Some of the apparent disagreement regarding lobar and total atelectases appears to be due to the fact that not all investigators have differentiated those cases which showed persistent cavitation from those which did not show it. The former type of case appears to be the really dangerous one and is associated with a high complication and mortality rate.

In our series of 162 A.P.s, atelectases (segmental, lobar or total) occurred in 58 (36 per cent.) and were distributed as follows: 28 per cent. of Group I, 43 per cent. of Group II and 23 per cent. of Group III.

Of the 58 atelectases, 51 were segmental, 5 were lobar and 2 were total. Of the 5 patients with lobar atelectases, 2 did well as a whole and 2 did badly; only in 1 case could the lung finally be regarded as good, 2 were definitely

bad and 1 developed fibrothorax. Of the 2 patients with total atelectasis of the lung, one died and the other did well following chemotherapy.

The results as regards the patient as a whole were very similar in the 51 cases who had segmental atelectases and the 104 cases who did not develop atelectasis. Thus, 65 per cent. did well and 13 per cent. did badly among those with segmental atelectases as compared with 74 per cent. and 12 per cent. respectively in the non-atelectatic group. As regards the lung, good results occurred less frequently with segmental atelectasis (29 per cent. as compared with 65 per cent.) and fibrothorax occurred more frequently (27 per cent. as compared with 5 per cent.). Bad results with the lung occurred with similar frequency whether there was segmental atelectasis (13 per cent.) or no atelectasis (15 per cent.). (See Tables IV and V Appendix.)

Comparing 19 cases in which atelectasis was the only complication of the A.P. with the non-atelectatic cases, the results with the patient as a whole were identical (74 per cent. good results). The good results with the lungs were also similar in these two groups (52 per cent. and 65 per cent. respectively); fibrothorax, however, was commoner among the atelectatic cases (16 per cent. as compared with 5 per cent.). (See Table VI Text.)

TABLE VI. (Text).—SHOWING END RESULTS IN RELATION TO ATELECTASIS OR EFFUSION, COMPLICATED OR UNCOMPLICATED

	No. of A.Ps.	RESULTS				
		Patient		*Lung*		
		Good	*Bad*	*Good*	*Bad*	*Fibrothorax*
Uncomplicated effusion	9	(66) 6	(22) 2	(33) 3	(22) 2	(22) 2
Complicated effusion	27	(63) 17	(15) 4	(18) 5	(22) 6	(33) 9
Atelectasis+effusion	23	(61) 14	(13) 3	(17) 4	(22) 5	(35) 8
Atelectasis+complications	39	(57) 22	(20) 8	(15) 6	(23) 9	(31) 12
Atelectasis only	19	(74) 14	(11) 2	(52) 10	(11) 2	(16) 3

Complications=complications other than atelectasis or effusion, such as hæmothorax, spontaneous pneumothorax, tension cavity.
( )=Percentage.

When cases with atelectasis were further complicated by pleural effusion, good results with the lung were less frequent (17 per cent.) and fibrothorax occurred more frequently (35 per cent.) These figures were similar, whether or not other additional complications were present. Effusions, therefore, appeared to play a big part in finally producing bad lungs and fibrothorax in these cases.

Tension Cavities

As tension cavities, like atelectases, indicate the presence of bronchial disease, cases showing them were analysed further.

Eight patients in all had tension cavities (1 bilaterally) and segmental atelectasis was present in 6. Two of these patients showing atelectasis and one other died; on the other hand, 2 with atelectasis and 1 other did well as a whole. It is worth noting that of these 3 patients only 1 had bilateral disease and no spreads occurred after A.P. induction, whereas in all the other cases the disease was either bilateral at the outset or became so as a result of spread.

The results indicate the serious nature of persistent tension cavities which, as one would expect, often lead to spread of disease.

3. Effusions and Empyemata

From a review of the literature—Allen and Kelly (1945), Eglee and Jones (1937), Morriss (1942), Mitchell (1951), Trail and Stockman (1932), Shaw (1933), Scadding *et al.* (1951), Foster-Carter *et al.* (1952), Harris *et al.* (1952) and Snell (1953)—it seems that in the pre-chemotherapeutic era serous effusions occurred in approximately 50 per cent. of A.P.s but did not influence the prognosis except in contributing to unexpandable lungs; empyema occurred in an average of 10 per cent., half of whom died.

Factors predisposing to the incidence of effusion in different series have been shown to be extensive or dense disease, the presence of adhesions and the occurrence of atelectases. Additional factors in the production of empyemata appear to be lack of initial bed rest, lack of uniform control (Young, 1949), and most important, the presence of persistently open cavities. The latter carries a very high mortality rate, as shown by Bignall (1950) and by Foster-Carter *et al.* (1952).

With better control and chemotherapy the incidence of empyema at many centres has fallen to negligible proportions. Snell (1953) reported none in 455 A.P.s at Colindale since 1947, and Wright (1952) reported a similar absence of empyema in a large series of A.P.s at Baguley since 1947.

For purposes of analysis an effusion was defined as clear serous fluid rising above the level of the dome of the diaphragm; a clear effusion containing tubercle bacilli was considered to be a potential empyema (Ellman, 1949), and only if the fluid was purulent and contained tubercle bacilli was it called an empyema.

Table VII (Text).—Showing Incidence of Effusion in Relation to Extent of Initial Disease

Effusions	*Group I A.P.s* 39	*Group II A.P.s* 93	*Group III A.P.s* 30	*Total*
Simple	(13) 5	(3) 3	(3) 1	(6) 9
Complicated	(13) 5	(20) 19	(10) 3	(16) 27
Total..	(26) 10	(23) 22	(13) 4	(22) 36

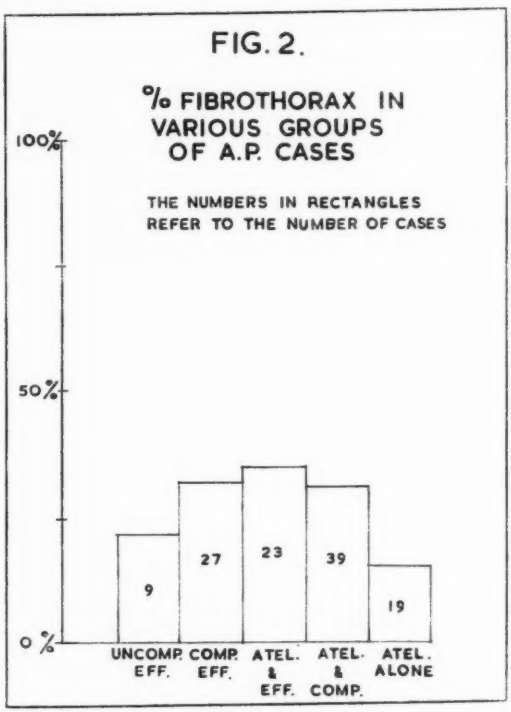
Figures=No. in Category.
( )=Percentage.

It is seen from Table VII (Text) that the incidence of effusion was not influenced by the initial extent of disease. On the other hand, there were more complications additional to effusion in Groups II and III than in Group I.

Effusions occurred in 36 out of 162 A.P.s and in a further 7 cases potential empyemata were recorded; the incidence of frank empyema in the series was nil. All the patients with potential empyemata recovered; the results as regards the patient as a whole were good in 5 instances and no bad results were obtained. With the lungs, however, there were only 2 good results, 2 others were bad and 1 developed fibrothorax: additional complications—*i.e.*, atelectasis (one with a tension cavity), tension cavity and spontaneous pneumothorax —occurred in 4 cases.

The tables show that the good and bad results as regards the patient were very similar whether or not effusions occurred, even if there were other additional complications, but the results with the lungs were less frequently good (mainly from a functional point of view) when effusions occurred, and if there were additional complications there was a greater chance of a fibrothorax occurring. (See Table VII Text, Tables VIII and IX Appendix.)

Of the 58 cases in which atelectasis was present 23 developed effusions (45 per cent.), whereas among the 104 cases in which there was no atelectasis, effusions occurred in only 13 (13 per cent). Among the atelectatic cases which developed effusions there did not appear to be any definite correlation with the initial extent of disease.



Of the 9 A.P.s with tension cavities, 6 developed effusions, and in 5 of them atelectasis was also present. The combination of atelectasis and tension cavity appears to be a prominent cause of effusion.

Fibrothorax followed effusion alone or atelectasis alone much less frequently than complicated effusions or than atelectasis occurring in combination with effusion or other additional complications. (See Fig. 2, based on Table VI in the Text.)

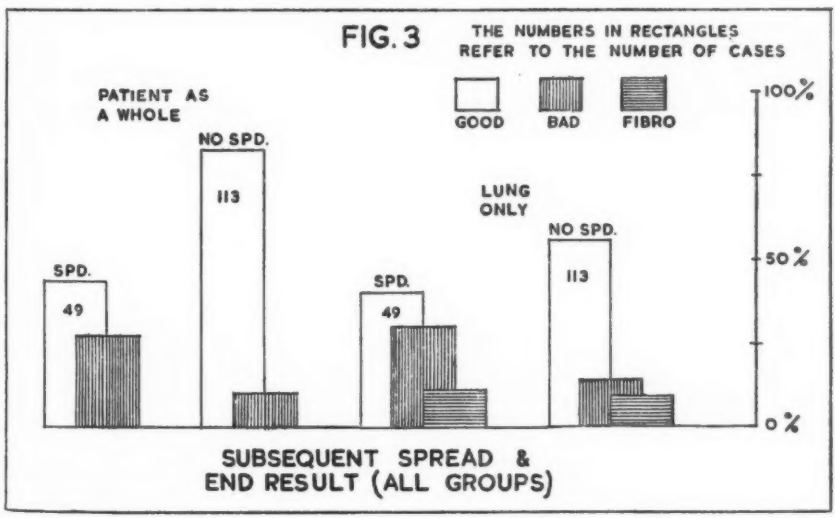
4. Contralateral Disease

Burrell (1933) and Hartley, Wingfield and Burrows (1935) indicated that the presence of contralateral disease in an A.P. case seriously affected the prognosis. Later investigators, notably Foster-Carter *et al.* (1952), have shown that this adverse effect is probably due to the greater initial extent of disease rather than to its anatomical situation. The occurrence of spread to the opposite side is more serious when the initial disease is extensive (Shaw, 1933) or when the spread is severe (Morriss, 1942).

In our series, investigation of the effects of contra-lateral disease could only be done in connection with Group II cases, as all of Group III and none of Group I had bilateral disease.

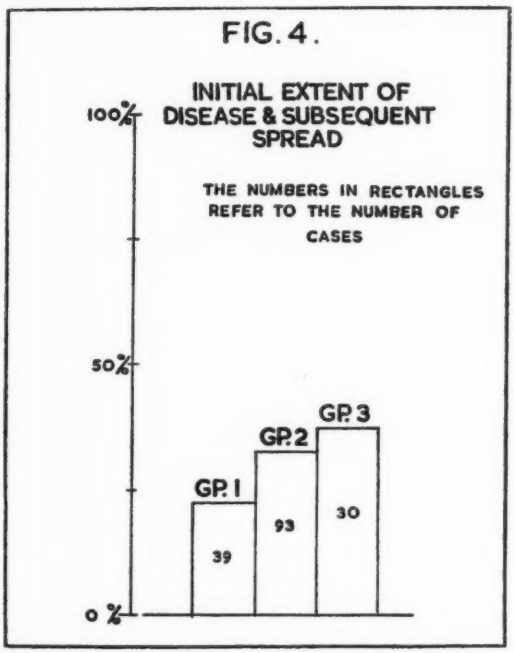
There were 93 A.P.s in Group II: these have been classified according to whether two or three zones were involved and these two groups were then subdivided into sub-groups with unilateral or bilateral disease.

It will be seen that there is very little difference between the results in the cases unilaterally or bilaterally involved initially, and the results follow more closely the initial extent of disease rather than whether one or both lungs were involved. When contra-lateral disease was such as to require a second A.P. the results on the whole were comparable with those of the series as a whole. (See Table X Appendix.)



Spread of Disease

Spread of disease occurred in 33 per cent. of Group I cases, in 52 per cent. of Group II and in 58 per cent. of Group III. A good result was obtained more often if no spread occurred (82 per cent.) than if there had been spread of disease (44 per cent.); the bad results for the patient were 7 per cent. and 27 per cent. respectively. The difference in the results for the lung alone were not so marked. (See Figs. 3 and 4.)



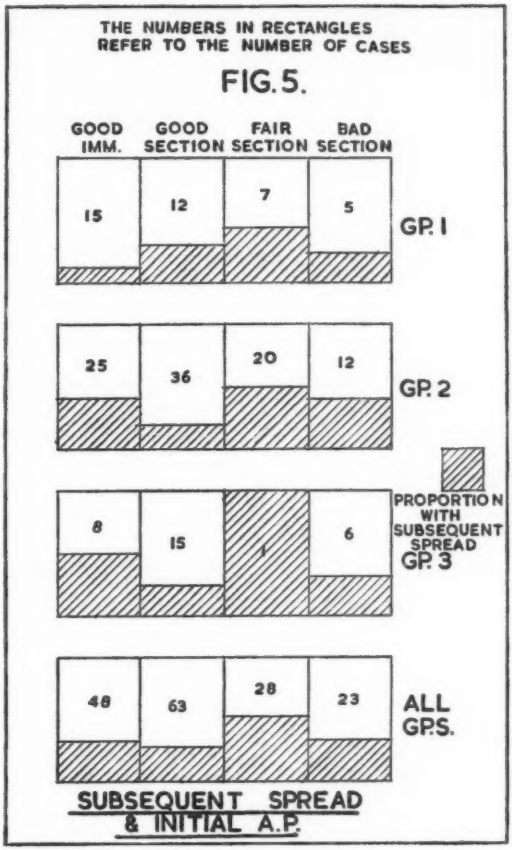
Relation between Quality of Initial A.P. and Subsequent Spread of Disease

It is seen that there is no real relationship between the quality of the initial A.P. and the occurrence of subsequent spread of disease. (See Fig. 5.)

Atelectasis and Spread of Disease

Spread of disease occurred in 24 out of 58 cases showing atelectasis (41 per cent.), and in only 28 out of 104 cases which did not have atelectasis (26 per cent.); this difference is suggestive.

Good results with regard to the patient as a whole were obtained less frequently among the 24 cases of atelectasis whose disease spread (29 per cent.) than for all cases of spread (44 per cent.), or spreads in non-atelectatic cases (57 per cent.). The results regarding the lung showed an even greater difference, good results being obtained in only 13 per cent. of atelectatic cases with



spread as compared with 64 per cent. of those with spread but no atelectasis. It may be relevant that the initial A.P. was bad in more cases where there was atelectasis and subsequent spread than in other cases in the series. (See Table XI, Text.)

5. Re-expansion

Packard (1932), Aycock and Keller (1942) and Harris *et al.* (1952) concluded that re-expansion of a lung after A.P. is unrelated to reactivation of disease. Cold (1937) also showed that the relapse rate was not affected by the duration of collapse. Harris *et al.* (1952) and Mitchell (1951) felt that A.P.s should not be continued for longer than three years, and the latter considered that A.P.s maintained for longer tended to produce severe fibrothoraces, although he recognised that empyema was a more potent cause.

TABLE XI (Text).—RESULTS IN CASES OF ATELECTASIS WITH SUBSEQUENT SPREAD COMPARED WITH CASES WHERE THERE WAS SUBSEQUENT SPREAD BUT NO ATELECTASIS

	Nos.	Patient		Lung			Initial A.P.				
		Good	Bad	Good	Bad	Fibro-thorax	Good Initially	Good after	Fair after	Bad after	A.P. complicated
Group I:											
Atelectasis		(50)	(0)	(0)	(0)	(50)	(0)	(100)	(0)	(0)	(50)
	2/11	1	0	0	0	1	0	2	0	0	1
No atelectasis		(43)	(29)	(57)	(29)	(14)	(14)	(29)	(43)	(14)	(57)
	7/28	3	2	4	2	1	1	2	3	1	4
Group II:											
Atelectasis		(25)	(37)	(13)	(31)	(25)	(6)	(19)	(44)	(31)	(56)
	16/40	4	6	2	5	4	1	3	7	5	9
No atelectasis		(62)	(25)	(69)	(25)	(0)	(56)	(25)	(19)	(0)	(50)
	16/53	10	4	11	4	0	9	4	3	0	8
Group III:											
Atelectasis		(33)	(33)	(17)	(50)	(0)	(33)	(33)	(0)	(33)	(33)
	6/7	3	2	1	3	0	3	2	0	2	2
No atelectasis		(60)	(0)	(60)	(20)	(0)	(40)	(40)	(20)	(0)	(100)
	5/23	3	0	3	1	0	2	2	1	0	5
Total:											
Atelectasis		(29)	(33)	(13)	(33)	(21)	(13)	(29)	(29)	(29)	(50)
	24/58	7	8	3	8	5	3	7	7	7	12
No atelectasis		(57)	(21)	(64)	(25)	(4)	(43)	(29)	(25)	(4)	(60)
	28/104	16	6	18	7	1	12	8	7	1	17

( )=Percentage.

Whether an A.P. is discontinued deliberately or abandoned because of being contra-selective or on account of obliteration or complications, during the first four years after induction, the end result as regards the patient as a whole does not appear to be affected to any appreciable extent. This is probably because all the poor and risky A.P.s have by then been eliminated. The figures for the later years are too small to allow comment.

Up to three years increase in duration of A.P. was associated with an increase in proportion of good results. This applied to cases that were abandoned as well as to those terminated deliberately.

Duration of A.P.	No. of A.P.s	Deliberately discontinued	Enforced abandonment
1 year	35	5	30
2 years	42	14	28
3 years	36	23	13
4 years	29	24	5
5 years	12	12	0
More than 5 years	8	7	1

As far as the lung is concerned, the results when the A.P. was abandoned were less likely to be good, usually because of pleural fibrosis. The chance of obtaining a good lung increased progressively up to the fourth year and the chance of a fibrothorax occurring was greatest in the second and third years when effusions were most common. There is nothing in our figures to support the view that an A.P. of long duration will *per se* give rise to fibrothorax.

Examination of the Bad Results

Bad results with regard to the patient as a whole occurred as follows:

Group I. 2/39 Patients (5 per cent.)
Group II. 16/79 Patients (20 per cent.)
Group III. 4/22 Patients (18 per cent.)

Of the 22 A.P.s in which the results with the patients were bad, only 7 were good, either immediately after induction or following adhesiotomy. Subsequent spread of disease occurred in all but 7 cases, and all had bilateral disease at the outset or subsequently; sputum conversion was rare and only occurred in 1 instance. Only 8 cases were completely free from any complications of the A.P. and spreads occurred in only 4 of these. The 4 patients in whom no complications of the A.P. nor spread of disease occurred were completely unco-operative people who repeatedly discharged themselves from hospital and failed to follow any instructions or advice, and the bad results cannot be dissociated from these factors.

Discussion

Indications for A.P.

In 1922 Burrell and MacNalty gave as the indications for induction of A.P. in pulmonary tuberculosis:

1. Unilateral disease which was still active after six months of medical treatment.
2. Bilateral disease but less than one-third of the better lung involved.
3. Recurrent hæmoptysis, the source being known.
4. Pleural effusion (replacement) particularly if the underlying lung was diseased.

These indications continued to operate with no appreciable modification for the next twenty years, although spread of disease to larynx or intestine was regarded later as a further indication, and bilateral collapse for cavitating disease in both lungs had become more common.

At the present time we have to decide whether in fact an A.P. should be induced at all. Our figures, which represent patients who have not received chemotherapy in conjunction with A.P. treatment, showed that complications were infrequent when the initial disease was not extensive and when a good A.P. was obtained. Moreover, in no case did empyema occur, and whilst a number of fibrothoraces resulted from complications, often they did not interfere with the healing process and the return of the patient to a normal life.

It is highly probable that with the use of bed rest and chemotherapy before induction of the A.P. (and at any subsequent time indicated) the proportion of complications would be even further reduced.

It is now recognised that alternative methods of treatment including prolonged antibiotic therapy have diminished the indications for A.P.* None the less, we consider A.P. to be a useful form of treatment under certain conditions set out below and we agree with Foster Carter (personal communication) that at the present time there is a real danger that this useful form of treatment will fall into disuse because the younger generation is not being trained in the management of pneumothorax.

We consider, therefore, that an A.P. should be induced under the following conditions providing there are no contra-indications (see below).

1. In cases of exudative disease, especially in the upper zones, with or without cavitation, which have not responded to a satisfactory extent on rest, postural treatment and chemotherapy in a reasonble time.
2. In young subjects with low natural resistance an A.P. is seriously considered, even after cavity closure has been achieved by conservative methods, or in the absence of initial cavitation.

Contra-indications

1. The presence of endobronchitis as evidenced by bronchoscopic appearances, major atelectases or tension cavities.
2. Very extensive disease with cavitation.
3. Localised rigid fibrotic disease with bronchiectasis.
4. The presence of solid foci (tuberculomata).
5. Peripherally placed, thin-walled cavities.
6. Limited respiratory reserve due either to pulmonary causes (emphysema, fibrosis, etc.) or to systemic causes (cardiac disease, renal disease, etc.).

Termination of A.P.

Our experience is similar to that of others and we consider it unwise to persist with an A.P. that is contra-selective, does not achieve cavity closure, or is associated with lobar or total atelectasis or appreciable fluid. If a potential empyema occurs the lung should be re-expanded and the pleural space emptied and sterilised as rapidly as possible.

Termination of a selective A.P. in a satisfactory case must depend on individual factors, but notably on quiescence (as shown by cavity closure,

* Since this investigation was started the current tendency is towards even more prolonged chemotherapy. Obviously, a proper assessment of the results in these cases will not be forthcoming for some years. In the meantime, it is largely a question of balancing the risks of drug reaction and resistant bacilli from chemotherapy against the risks of an A.P., in cases where there is a choice between the two methods of treatment. It is probable in the end they may prove to be complementary as both would be desirable where the present orthodox course of rest and chemotherapy may be thought inadequate to ensure continued quiescence. This might be particularly applicable in patients with poor resistance and bad environmental conditions.

absence of positive sputum on culture, radiological appearances and general health) over a period of from one to two years. When the initial disease is extensive, response to treatment is slow, natural resistance is low, temperament or environmental factors are adverse, the longer period is indicated.

The use of chemotherapy in conjunction with A.P. treatment is likely to confirm the validity of these opinions.

Fibrothorax is almost invariably preceded by pleural complications, although a few cases follow uncomplicated atelectases: the presence of minimal fluid in the latter cannot be excluded with certainty. Although respiratory reserve is diminished, the healing of disease is not hampered and the patients usually return to normal life. One would expect some disability to follow from this in later life, but our clinical impression, shared with others (Foster Carter, personal communication), is that these patients, often now well into middle age, are as free of symptoms and as well adapted to their daily activities as those without fibrothorax.

Possible disadvantages that might arise if pulmonary or cardiac disease should subsequently develop, or the pulmonary tuberculosis recur, must, however, be borne in mind. Definite conclusions await large-scale controlled investigation. It was not possible to foretell by the amount of fluid the presence or absence of tubercle bacilli in it, the duration of its persistence, the rapidity of its return after aspiration, or the presence of additional complications, which cases would develop fibrothorax. As fibrothorax followed one-third of all cases showing appreciable fluid, it would be reasonable to terminate the A.P. if such a complication occurs; if the disease is inactive at this time the risk of fibrothorax is not justified, whereas if the disease is still active, persisting with the A.P. is potentially dangerous.

Summary

Artificial pneumothorax treatment during the last thirty years has been reviewed and its diminishing use since the advent of chemotherapy is noted.

The results of such treatment, not in conjunction with chemotherapy, in 152 patients are presented.

They indicate that even without chemotherapy good results may be anticipated, provided cases are carefully selected and managed under uniform control.

Sources of danger were, notably, tension cavities, major atelectases, spread of disease during treatment and effusions. These factors are likely to be prevented by chemotherapy.

It may, therefore, be anticipated that with prolonged chemotherapy the results of artificial pneumothorax treatment will be even better and its continued use in selected cases appears more than justified.

Cause and effect of fibrothorax and optimum duration of artificial pneumothorax treatment are discussed.

We should like to express our indebtedness to Dr. A. F. Foster Carter for most helpful criticism of the manuscript.

TABLE I (Appendix).—SHOWING RESULTS IN RELATION TO AGE, SEX AND INITIAL EXTENT OF DISEASE (+ dead)

Group	Age (years)	Sex	RESULT							Total effusion	Simple effusion	RESULT					Complicated effusion	RESULT				
			Patient			Lung						Patient		Lung				Patient		Lung		
			Good	Bad	Fair	Good	Bad	Fibro-thorax	Fair			Good	Bad	Good	Bad	Fibro-thorax		Good	Bad	Good	Bad	Fibro-thorax
I.	Under 15	M 2	1		1	1			1													
		F 0																				
	15-35 ..	M 18	16	1	1	11		4	3	6	3	2	1	1		1	3	2		1		2
		F 15	10	+1	4	8	2	2	3	4	2	1	1		1	1	2	2		1		
	Over 35	M 1			1			1														
		F 3	3			2			1													
Total Group I		39	30	2	7	22	2	7	8	10	5	2	2	1	1	2	5	4		2		2
II.	Under 15	M 2	2			2																
		F 2	2			1			1													
	15-35 ..	M 43	31	+6	6	24	7	5	7	13	2	2		2			11	7	1	2	1	4
		F 35	25	+5	5	16	4	7	8	7	1	1					6	4		1	1	3
	Over 35	M 6	3	++3		4	2			1							1		1		1	
		F 5	2	2	1	1	3		1	1							1	1				
Total Group II		93	65	16	12	48	16	12	17	22	3	3		2			19	12	2	3	3	7
III.	Under 15	M 0																				
		F 0																				
	15-35 ..	M 16	9	+3	4	6	5	1	4	2	1				1		1		1		1	
		F 12	7	+1	4	6	2		4	2							2	1	1		2	
	Over 35	M 2	2			1			1													
		F 0																				
Total Group III		30	18	4	8	13	7	1	9	4	1				1		3	1	2		3	
TOTAL ..		162	113	22	27	83	25	20	34	36	9	6	2	3	2	2	25	17	4	5	6	9

TABLE II (Appendix).—SHOWING END RESULT FOR PATIENT AS A WHOLE IN RELATION TO TYPE OF INITIAL A.P. AND EXTENT OF INITIAL DISEASE

A.P.	*Group I*		*Group II*		*Group III*		*All*	
	Good	*Bad*	*Good*	*Bad*	*Good*	*Bad*	*Good*	*Bad*
Good immediately	(80) 12/15	(0) 0/15	(76) 19/25	(16) 4/25	(50) 4/8	(0) 0/8	(73) 35/48	(8) 4/48
Good after adhesion section ..	(75) 9/12	(0) 0/12	(92) 33/36	(6) 2/36	(80) 12/15	(7) 1/15	(86) 54/63	(5) 3/63
Fair after adhesion section ..	(57) 4/7	(28) 2/7	(45) 9/20	(35) 7/20	(0) 0/1	(0) 0/1	(47) 13/28	(32) 9/28
Bad after adhesion section ..	(100) 5/5	(0) 0/5	(33) 4/12	(25) 3/12	(33) 2/6	(50) 3/6	(48) 11/23	(26) 6/23

Figures=No. in Category/No. at risk.
( )=Percentage.

TABLE III (Appendix).—SHOWING END RESULT FOR LUNG ONLY IN RELATION TO TYPE OF INITIAL A.P. AND EXTENT OF INITIAL DISEASE

A.P.	*Group I*			*Group II*			*Group III*			*All*		
	Good	*Bad*	*Fibro-thorax*	*Good*	*Bad*	*Fibro-thorax*	*Good*	*Bad*	*Fibro-thorax*	*Good*	*Bad*	*Fibro-thorax*
Good immediately ..	(60) 9/15	(7) 1/15	(27) 4/15	(72) 18/25	(8) 2/25	(8) 2/25	(50) 4/8	(25) 2/8	(0) 0/8	(15) 31/48	(10) 5/48	(12) 6/48
Good after adhesion section	(58) 7/12	(0) 0/12	(17) 2/12	(67) 24/36	(8) 3/36	(8) 3/36	(60) 9/15	(14) 2/15	(0) 0/15	(64) 40/63	(8) 5/63	(8) 5/63
Fair after adhesion section	(57) 4/7	(14) 1/7	(0) 0/7	(20) 4/20	(35) 7/20	(20) 4/20	(0) 0/1	(0) 0/1	(0) 0/1	(28) 8/28	(28) 8/28	(14) 4/28
Bad after adhesion section	(40) 2/5	(0) 0/5	(20) 1/5	(17) 2/12	(33) 4/12	(25) 3/12	(0) 0/6	(50) 3/6	(17) 1/6	(17) 4/23	(30) 7/23	(22) 5/23

Figures=No. in Category/No. at risk.
( )=Percentage.

TABLE IV (Appendix).—SHOWING END RESULTS FOR PATIENT AS A WHOLE IN RELATION TO EXTENT OF INITIAL DISEASE AND PRESENCE OR ABSENCE OF SEGMENTAL, LOBAR, TOTAL, OR COMPLICATED ATELECTASIS

Atelectasis	*Group I*		*Group II*		*Group III*		*Total*	
	Good	*Bad*	*Good*	*Bad*	*Good*	*Bad*	*Good*	*Bad*
Segmental	(91)	(0)	(61)	(17)	(40)	(20)	(65)	(13)
	10/11	0/11	21/35	6/35	2/5	1/5	33/51	7/51
Lobar	0	0	(25)	(50)	(100)	(0)	(40)	(40)
			1/4	2/4	1/1	0/1	2/5	2/5
Whole lung	0	0	(100)	(0)	(0)	(100)	(50)	(50)
			1/1	0/1	0/1	1/1	1/2	1/2
Atelectasis total	(91)	(0)	(57)	(20)	(43)	(29)	(62)	(17)
	10/11	0/11	23/40	8/40	3/7	2/7	36/58	10/58
Non-atelectasis	(71)	(7)	(79)	(15)	(65)	(9)	(74)	(12)
	20/28	2/28	42/53	8/53	15/23	2/23	77/104	12/104
Atelectasis complicated ..	(83)	(0)	(53)	(21)	(40)	(40)	(56)	(20)
	5/6	0/6	15/28	6/28	2/5	2/5	22/39	8/39
Atelectasis and effusion ..	(75)	(0)	(59)	(12)	(50)	(50)	(60)	(13)
	3/4	0/4	10/17	2/17	1/2	1/2	14/23	3/23

Figures=No. in Category/No. at risk.
( )=Percentage.

TABLE V (Appendix).—SHOWING END RESULTS FOR LUNG ONLY IN RELATION TO EXTENT OF INITIAL DISEASE AND PRESENCE OR ABSENCE OF SEGMENTAL, LOBAR, TOTAL, OR COMPLICATED ATELECTASIS

Atelectasis	*Group I*			*Group II*			*Group III*			*Total*		
	Good	*Bad*	*Fibro-thorax*	*Good*	*Bad*	*Fibro-thorax*	*Good*	*Bad*	*Fibro-thorax*	*Good*	*Bad*	*Fibro-thorax*
Segmental	(45)	(0)	(18)	(25)	(17)	(31)	(20)	(40)	(20)	(24)	(15)	(27)
	5/11	0/11	2/11	9/35	5/35	11/35	1/5	2/5	1/5	15/51	9/51	14/51
Lobar				(25)	(50)	(25)	(0)	(0)	(0)	(20)	(40)	(20)
	0	0	0	1/4	2/4	1/4	1/1	0/1	0/1	1/5	2/5	1/5
Whole lung				(0)	(100)	(0)	(0)	(100)	(0)	(0)	(100)	(0)
	0	0	0	0/1	1/1	0/1	0/1	1/1	0/1	0/2	2/2	0/2
Atelectasis total	(45)	(0)	(18)	(25)	(20)	(30)	(14)	(43)	(14)	(28)	(19)	(26)
	5/11	0/11	2/11	10/40	8/40	12/40	1/7	3/7	1/7	16/58	11/58	15/58
Non-atelectasis	(61)	(7)	(18)	(72)	(15)	(0)	(49)	(17)	(0)	(65)	(13)	(5)
	17/28	2/28	5/28	38/53	8/53	10/53	12/23	4/23	0/23	67/104	14/104	5/104
Atelectasis complicated	(33)	(0)	(33)	(14)	(21)	(36)	(0)	(60)	(0)	(15)	(23)	(30)
	2/6	0/6	2/6	4/28	6/28	10/28	0/5	3/5	0/5	6/39	9/39	12/29
Atelectasis and effusion	(50)	(0)	(25)	(12)	(18)	(41)	(0)	(100)	(0)	(17)	(22)	(35)
	2/4	0/4	1/4	2/17	3/17	7/17	0/2	2/2	0/2	4/23	5/23	8/23

Figures=No. in Category/No. at risk.
( )=Percentage.

TABLE VIII (Appendix).—SHOWING RESULTS FOR PATIENTS AS A WHOLE IN RELATION TO PRESENCE OF SIMPLE OR COMPLICATED EFFUSION

	Group I		*Group II*		*Group III*		*Total*	
Effusion	*Good*	*Bad*	*Good*	*Bad*	*Good*	*Bad*	*Good*	*Bad*
Simple	(60)	(40)	(100)	(0)	(0)	(0)	(66)	(22)
	3/5	2/5	3/3	0/3	0/1	0/1	6/9	2/9
Complicated	(80)	(0)	(63)	(10)	(33)	(66)	(63)	(33)
	4/5	0/5	12/19	2/19	1/3	2/3	17/27	9/27
Total effusion	(70)	(20)	(68)	(9)	(25)	(50)	(64)	(30)
	7/10	2/10	15/22	2/22	1/4	2/4	23/36	11/26
No effusion	(79)	(0)	(70)	(20)	(65)	(12)	(71)	(14)
	23/29	0/29	50/71	14/71	17/26	3/36	90/126	17/126

Figures=No. in Category/No. at risk.
( )=Percentage.

TABLE IX (Appendix).—SHOWING RESULTS FOR LUNG ONLY IN RELATION TO PRESENCE OF SIMPLE OR COMPLICATED EFFUSION

	Group I			*Group II*			*Group III*			*Total*		
Effusion	*Good*	*Bad*	*Fibro-thorax*	*Good*	*Bad*	*Fibro-thorax*	*Good*	*Bad*	*Fibro-thorax*	*Good*	*Bad*	*Fibro-thorax*
Simple	(20)	(20)	(40)	(66)	(0)	(0)	(0)	(100)	(0)	(33)	(22)	(22)
	1/5	1/5	2/5	2/3	0/3	0/3	0/1	1/1	0/1	3/9	2/9	2/9
Compli-	(40)	(0)	(40)	(16)	(16)	(37)	(0)	(100)	(0)	(19)	(22)	(33)
cated	2/5	0/5	2/5	3/19	3/19	7/19	0/3	3/3	0/3	5/27	6/27	9/27
Total ..	(30)	(10)	(40)	(23)	(14)	(32)	(0)	(100)	(0)	(22)	(22)	(30)
	3/10	1/10	4/10	5/22	3/22	7/22	0/4	4/4	0/4	8/36	8/36	11/36
None ..	(56)	(4)	(10)	(60)	(18)	(7)	(50)	(12)	(4)	(60)	(14)	(7)
	19/29	1/29	3/29	43/71	13/71	5/71	13/26	3/26	1/26	75/126	17/126	9/126

Figures=No. in Category/No. at Risk.
( )=Percentage.

TABLE X (Appendix).—SHOWING RESULTS IN RELATION TO INITIALLY BILATERAL OR UNILATERAL DISEASE AND ACCORDING TO WHETHER TWO OR THREE ZONES WERE INVOLVED (GROUP II CASES ONLY)

		Patient (93 A.P.s)		*Lung*		
No. of Zones involved	*Bilateral cases*	*Good*	*Bad*	*Good*	*Bad*	*Fibrothorax*
2	38	(74) 28	(16) 6	(71) 27	(16) 6	(8) 3
3	23	(60) 14	(26) 6	(30) 7	(22) 5	(13) 3
Total ..	61	(69) 42	(20) 12	(56) 34	(18) 11	(10) 6
No. of zones involved	*Unilateral cases*					
2	20	(80) 16	(15) 3	(50) 10	(15) 3	(15) 3
3	12	(58) 7	(8) 1	(33) 4	(17) 2	(25) 3
Total ..	32	(72) 23	(13) 4	(44) 14	(16) 5	(19) 6

Figures=No. of cases.
( )=Percentages.

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TUBERCULOUS HYPOTENSION

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Low blood pressure may exist in tuberculous patients without indicating the presence of either Addison's disease or severe hæmorrhage and so may lead to errors of diagnosis and management. Fishberg (1932) described hypotension in tuberculous cases and regarded it as a sign of poor prognosis, though if the patient improved the blood pressure rose. This observation cannot have attracted wide recognition, for twenty-two years later Clarke *et al.* (1954) found four patients out of a series of 109 seen in Sanatorium who had been wrongly diagnosed as having Addison's disease, for which two had been treated. The present paper records observations made on hypotensive patients who were receiving treatment for pulmonary tuberculosis.

To define hypotension it is first necessary to state what a normal blood pressure should be. Master *et al.* (1950) studied the records of routine physical examinations of 74,000 industrial workers of both sexes compiled in the U.S.A. during the last war. They found that the average systolic and diastolic blood pressures (in mm. Hg) at the ages of 20-24 were 122·9/76 for males and 115·7/71·7 for females, rising by the ages of 55-59 to 137·8/84 for males and 138·5/83·5 for females. Blood pressures showed considerable variation, and in young adults the lowest limit of normal was considered to be 105/62 in males and 100/60 in females. It was found that no less than 20 per cent. of all young women under the age of 25 had a blood pressure of 100/60 or less. For other individuals, blood pressures of this magnitude would represent significant hypotension.

The data given in this paper were taken from the case records of 191 patients with pulmonary tuberculosis treated in a General Hospital. Records were excluded if patients were dying or were found to be suffering from other conditions likely to affect the blood pressure, such as recent coronary infarction, nephritis or hypertension. Patients were of either sex and within the age limits of 18-60, and all admissions over a period of two and a half years were included in this survey.

For purposes of comparison, cases were divided into three groups based upon the extent of active disease and with the familiar radiological division of the chest into zones. Group I consisted of all patients with active lesions involving less than two zones of the lung, and with them were included simple pleural effusions and cases with quiescent disease admitted to hospital for other reasons. Group II consisted of patients with more extensive active disease but involving less than three zones of the lung fields. Group III consisted of all patients with active disease of three or more zones. There were 102 cases in Group I, 44 cases in Group II, and 45 cases in Group III. Blood pressures had been recorded at or near to the time of admission and from these readings the MEAN arterial pressure of each case was calculated. It was found that though there were a few hypotensives in Groups I and II, the bulk of such cases fell

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into Group III. This is well shown in Fig. 1. The normograms of Groups I and II have roughly the same configuration and correspond well to the frequency distribution curve that would be drawn round an expected mean arterial pressure of 100 mm. Hg. In Group III the mean pressures are markedly shifted to the left.

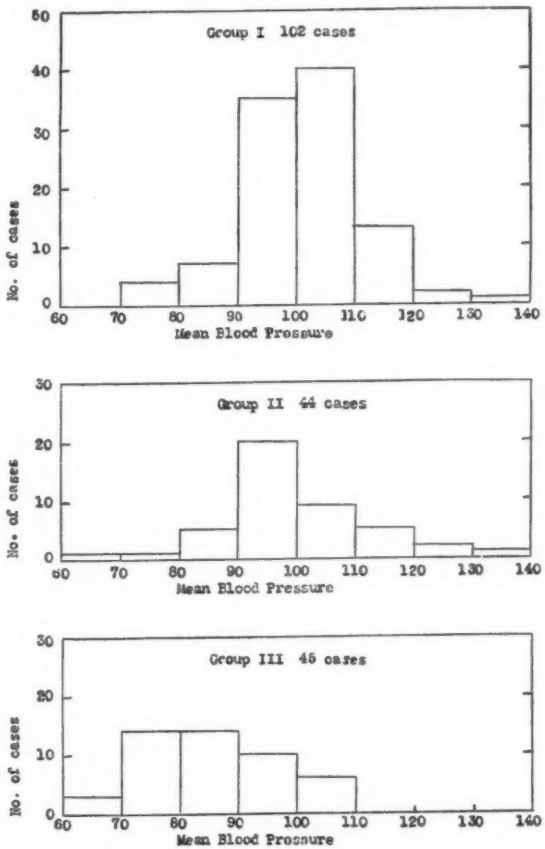

FIG. 1.—The mean blood pressure on admission of 191 cases of pulmonary tuberculosis.

Subsequent Behaviour of the Blood Pressure. There were 47 cases with mean arterial pressures at the time of admission of under 90 mm. Hg, and of these 22 cases (11·5 per cent.) had mean pressures of under 80 mm. Hg. Usually this meant pressures of around 85/65 and pulse pressures were frequently only 20-25 mm. Hg. Diastolic readings of under 50 mm. Hg were occasionally found. In many of these cases the blood pressure levels were not followed up, but in 15 cases further readings were taken over varying periods. Their mean blood pressure trends are shown in Fig. 2. As can be seen, in some patients the blood pressure soon rose to more normal levels, while in others it remained low or fell

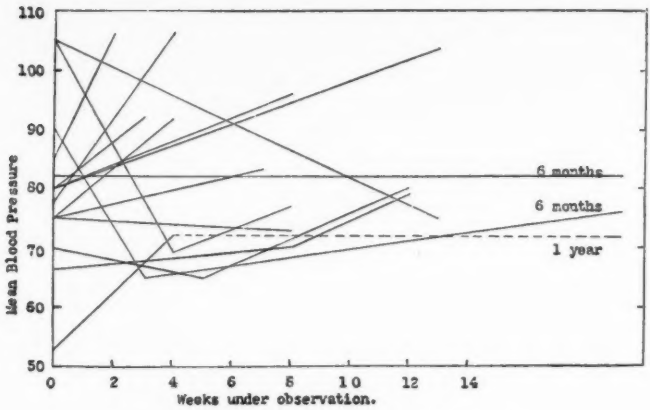

FIG. 2.—Mean blood pressure trends in 15 cases.

sharply despite treatment of their pulmonary disease. Five persistently hypotensive cases were studied in more detail and tests of suprarenal function were included. There case histories and serial blood pressure charts are given below.

CASE 1. Male, age 39, with long-standing bilateral upper zone cavities and with recent spread of tuberculous pneumonia. Active disease involving five zones of the lung fields. Also tuberculous laryngitis. Fig. 3 shows blood pressure readings taken over three months of treatment with steady clinical improvement.

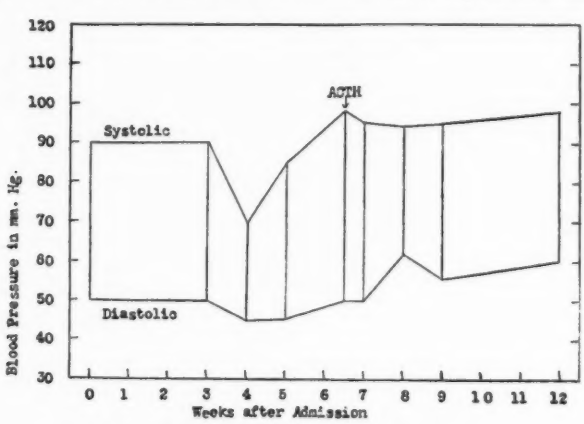

FIG. 3.—Serial blood pressure readings in Case 1.

CASE 2. Female, age 25, with old miliary tuberculous lesions affecting all zones of both lungs and with fresh tuberculous pneumonia and small cavities in the right upper zone. Sputum positive. Her serial blood pressures are shown in Fig. 4. In this patient a single normotensive reading occurred shortly after admission and at a time when she was gravely ill from secondary infection of the damaged lung. Thereafter she remained consistently hypotensive despite progressive clinical improvement and some improvement in the radiological appearances.

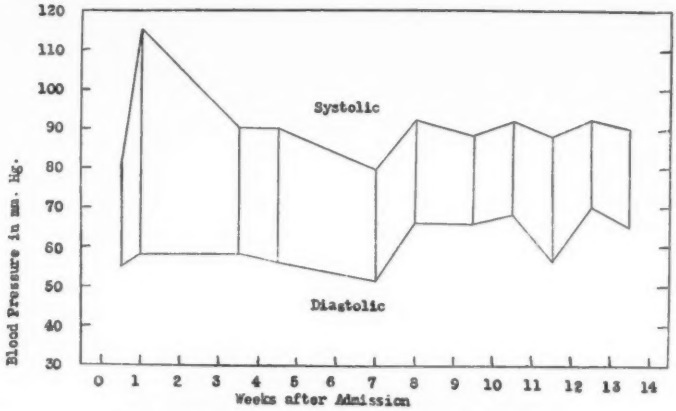

FIG. 4.—Serial blood pressure readings in Case 2.

CASE 3. Female, age 35, with chronic bilateral upper zone cavities and with a patch of fresh tuberculous pneumonia in the left upper zone. A hæmoptysis of 1 pint had occurred on the day before admission and her initial hypotension had been ascribed, probably incorrectly, to this. Her serial blood pressures are shown in Fig. 5. She made steady progress after admission with contraction of the cavities and clearing of the tuberculous pneumonia, but there was no change in her blood pressure, even when seen later as an out-patient and found in good general condition.

CASE 4. Male, age 52, with destruction and cavitation of the right upper lobe and the apex of the right lower lobe. He had also some patchy lesions with small cavities at the right base. His blood pressure was normal on admission but fell after a hæmoptysis of 25 oz. ten days later and remained low for many weeks. His serial blood pressures are shown in Fig. 6. He made steady improvement on chemotherapy, but his cavities did not close and he was ultimately allowed up while still hypotensive. His low blood pressure caused no symptoms. A pneumoperitoneum was then induced and his blood pressure rose to normal limits.

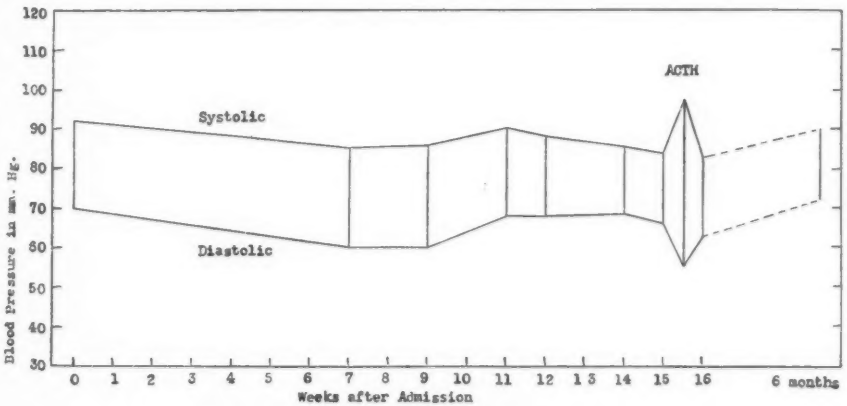

FIG. 5.—Serial blood pressure readings in Case 3.

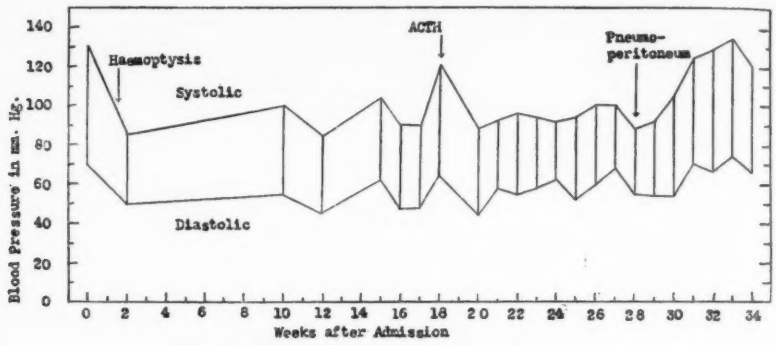

FIG. 6.—Serial blood pressure readings in Case 4.

CASE 5. Male, age 46, with chronic bilateral upper and mid-zone pulmonary tuberculosis with bilateral cavities. He had a swarthy complexion and slight brown pigmentation of the skin. There were small brown patches of pigment on the inner side of the gums. It was thought at first that he must be suffering from Addison's disease, but tests did not support this diagnosis and he was transferred to a Sanatorium after four weeks in hospital. There was reason to think that his pigmentation was familial. He did not settle well in Sanatorium and ultimately discharged himself. A year after his first admission he again entered hospital in transit for Sanatorium. His blood pressure, which is shown in Fig. 7, showed no change from the earlier figures, which had been consistently hypotensive. He died in Sanatorium several months later and no autopsy was undertaken.

Tests of Suprarenal Function. As it seemed possible that the persistent hypotension shown by these five patients was due to some defect of function of the suprarenal cortex, efforts were made to demonstrate this by means of the following tests:

The Kepler Water Load Test,

The Thorn Test of eosinophil depression,

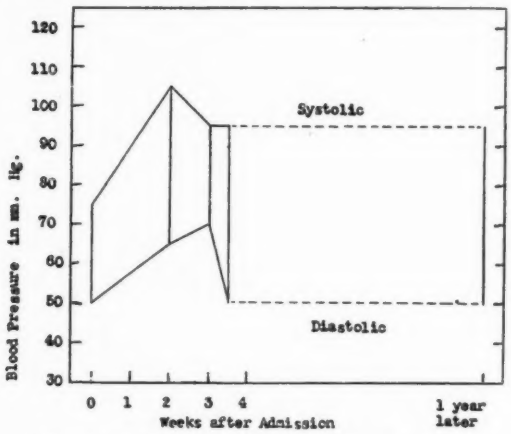

FIG. 7.—Serial blood pressure readings in Case 5.

Measurement of 17-Ketosteroids and 17-Ketogenic steroids before and after stimulation with ACTH.

The Kepler Test (Robinson *et al.*, 1941) was performed without modification, and if the largest day specimen of urine exceeded the volume of the night urine the test was regarded as negative.

The Thorn Test (Thorn *et al.*, 1948) showed the depression in the eosinophil count four hours after giving 25 mg. ACTH intramuscularly. The results of the test were regarded as valid, as no case showed an initial eosinophil reading of less than 100/cu. mm. (Strong, 1954).

In the measurement of basal 17-Ketosteroids and 17-Ketogenic steroids only a single twenty-four-hour specimen of urine was analysed. Prunty (1954) states that daily urinary levels may vary by as much as 33 per cent., but such variations would not have been significant in comparison with the large increases occurring especially in 17-Ketogenic steroid output as a result of ACTH stimulation. This stimulation was produced, as advised by Prunty (*op. cit.*), by injecting 20 mg. ACTH gel intramuscularly every twelve hours for forty-eight hours and collecting the urine excreted over the last twenty-four hours of the test. The levels of 17-Ketosteroids and 17-Ketogenic steroids were compared with basal levels, steroid estimations being made by the method of Norymberski *et al.* (1953).

The results of suprarenal function tests obtained in the five cases described above are given in Table 1. It will be noted that the Kepler test was negative in two cases and positive in three. The response to the Thorn test was marked in three cases, adequate in one and inadequate in the other (case 2), but here it should have been repeated. Basal 17-Ketosteroid excretion was low in four of these patients (normals for these age groups should be 8-23 mg./day in men and 5-18 mg./day in women (Prunty, *op. cit.*)). Even after ACTH, the rise in 17-Ketosteroids did not exceed normal limits. 17-Ketogenic steroids also showed low basal levels (normals 10-20 mg./day in men and 5-15 mg./day in women (Hubble, 1955)), but ACTH stimulation led to a brisk response with increases of more than 100 per cent., thus indicating a fully responsive suprarenal cortex. In case 5, ACTH was not used, but the basal 17-Ketosteroid level was high.

TABLE 1.—THE RESULTS OF TESTS FOR SUPRARENAL CORTICAL FUNCTION IN FIVE CASES OF HYPOTENSION

Case No.	*Sex*	*Age*	*Kepler factor*	*Thorn test eosinophils/cu. mm.*		*Urinary steroid excretion in mg. per 24 hours*			
						17-Ketosteroids		*17-Ketogenic steroids*	
				Before ACTH	*Four hours after ACTH*	*Before ACTH*	*During ACTH*	*Before ACTH*	*During ACTH*
1	M	39	19	150	22	8·8	17·0	8·5	37·0
2	F	25	6·2	100	77	2·9	5·6	6·4	31·9
3	F	34	Neg.	100	50	8·5	12·1	9·8	50·3
4	M	52	12	200	0	7·2	15·5	12·1	37·6
5	M	46	Neg.	200	44	20·5	—	—	—

Discussion

The response to ACTH stimulation in the patients described above proved that the suprarenal cortex was normal, even when other tests had left the matter in doubt. Although their cause is unknown, it is recognised that endocrine abnormalities do occur in pulmonary tuberculosis, an example being the development of amenorrhœa in some cases. Several groups of workers have investigated 17-Ketosteroid excretion. Clarke *et al.* (*op. cit.*) found that 37 per cent. of all advanced cases of tuberculosis seen at a Sanatorium had steroid levels of less than 50 per cent. of normal. Bastenie and Kowalewski (1950) and Rivoire *et al.* (1950) had found a decrease in 17-Ketosteroid excretion in tuberculous patients, the decrease varying with the severity of their disease. They considered that a toxic effect was exerted upon the suprarenal glands, but could find no lesions in them in cases coming to autopsy.

There is thus no evidence to show that either hypotension or low 17-Ketosteroid levels occurring in tuberculous patients are due to disease of the suprarenals. The frequency of hypotension must be fairly high, as it was found in 47 cases (22·5 per cent.) of the hospital admissions described at the beginning of this paper. Clarke *et al.* have shown that diminished 17-Ketosteroid excretion is also common. On the other hand, tuberculous Addison's disease is very rarely found in conjunction with active pulmonary tuberculosis, as was emphasised by Rowntree and Snell (1931). It is therefore clear that detailed tests of suprarenal efficiency should be carried out before Addison's disease is diagnosed in patients with pulmonary tuberculosis. In the absence of Addison's disease and where hypotension has been present serial blood pressure readings may give some help in assessing the response to treatment.

Summary

Observations were made on hypotension found in patients with extensive active pulmonary tuberculosis. Five persistently hypotensive cases showed no evidence of suprarenal cortical insufficiency.

I am indebted to Dr. D. K. Stevenson for permission to publish these cases, to Dr. C. J. Pinto for the eosinophil counts, and to the Sheffield and Region Endocrine Investigation Centre for the endocrine assays. Professor F. T. G. Prunty gave me helpful advice in the preparation of this paper.

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MANTOUX REACTION PATTERNS IN ACTIVE AND ARRESTED TUBERCULOSIS

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From time to time, considerable attention has been paid to the Mantoux reaction and other tests of cutaneous sensitivity to tuberculin, as possible indices of the activity of tuberculous infection. Investigation has principally been directed towards obtaining from such tests an index of prognosis—that is to say, information as to whether the disease present at any given time is in a stage of healing or progression, and if possible, a guide as to the rate and extent to which any change is likely to occur.

Detailed studies have led to the belief that there are certain quantitative differences between the cutaneous sensitivity of those with progressing and those with healing disease. Because of this, most studies—for example, Paczowski (1950), Turner (1953)—have resolved into a quantitative assessment of *level* of tuberculin sensitivity, that is to say a study of the dose required to elicit a certain reaction or of the magnitude of response to various doses; great importance, quite rightly, being attached to the methods of inoculation and measurement of the response. In most studies of this type, where the preoccupation has been with activity and its outcome, little attention has been paid to possible differences between active disease as a whole and fully healed disease—differences which might reveal a definite reaction of healing or of activity.

During the course of some quantitative Mantoux studies it appeared that it is possible sometimes to show an actual difference between the *kind* of response which can be elicited in active tuberculosis and that elicitable after the disease has healed. Again, the difference is not absolute, but the response seen in certain cases of active disease occurs sufficiently frequently to be of real interest and, moreover, has not been seen in the present small series in any person not suffering from clinically active tuberculosis. It would, on the basis of past experience, be remarkable indeed if this kind of response, so far restricted to those with active disease, were never seen in connection with healed lesions, but such a connection would certainly seem at least to be very rare.

Material

The subjects tested fell into two groups: those with arrested and those with clinically active tuberculosis. The arrested group consisted of 56 Mantoux-positive young Service men admitted to this hospital either for the investigation of some respiratory disease or for the investigation of some abnormality noted

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on mass miniature radiography. All were fully investigated and particular care was taken to exclude the possibility of active tuberculosis. The majority of those with radiological abnormalities who were symptom-free showed small healed and usually partially calcified tuberculous primary foci. Some were normal. The composition of this group is shown in Table I.

TABLE I.—COMPOSITION OF ARRESTED TUBERCULOSIS GROUP

Arrested tuberculosis, no other abnormality	23
Lobar and aspiration pneumonia	9
Acute and chronic bronchitis	9
Hæmoptysis, no evidence of active tuberculosis	7
Bronchiectasis	5
Pyrexia of unknown origin, no evidence of active tuberculosis	2
Multiple pulmonary infarcts	1
Total	56

Those with clinically active disease fell into three sub-groups:

(*a*) The remainder of the patients admitted for investigation—those who proved to be suffering from active tuberculosis. These had received no treatment other than bed-rest at the time of testing.

(*b*) Patients undergoing a full course of treatment, including streptomycin and isoniazid, for active tuberculosis. All showed evidence of continuing activity.

(*c*) Patients admitted with primary pleural effusions presumably of tuberculous ætiology. These patients had received no treatment at the time of testing other than aspiration and bed-rest.

Because tuberculin sensitivity may be modified by repeated testing (V. Pirquet, 1907; Ellerman and Erlandsen, 1909), and because this modification may correspond closely with the reaction to be described in certain tuberculous patients (O'Grady, to be published), no patient was included in the series who had been tuberculin tested more recently than three months before.

METHODS

Initial testing was carried out by the intradermal injection of 0·1 ml. of 1 in 10,000 dilution of Old Tuberculin into the forearm. Six mm. of easily palpable induration after 48 hours was regarded as a positive reaction, and if this did not result from the initial dose, testing was repeated in the same arm with 0·1 ml. of 1 in 1,000, and if necessary, 1 in 100, dilutions of old tuberculin. All the responses were examined daily, and later at two day intervals until all had disappeared. Ready prepared dilutions of human type Old Tuberculin manufactured and supplied to the Army by Messrs. Allen and Hanbury were used. All dilutions were used within a month of manufacture and stored, when not in use, at 4°C. A separate needle was used for each patient and a separate syringe for each dilution.

Apart from the exclusion of the small number of women tested, of technically unsatisfactory inoculations, and of those tested less than three months before,

the group reported is a consecutive series of patients for whom routine requests for Mantoux tests were received and who proved to be positive, with the addition, in the active group, of all the patients in two arbitrarily selected wards. Four patients with active tuberculosis failed to produce induration on testing with 100 T.U. No patient has been excluded from the series on any other grounds.

Measurement

Erythema and induration were measured separately, using an accurate boxwood ruler. Where there was asymmetry of erythema or induration or both, the maximum diameter and the diameter at right angles to this were both recorded. Two observers measured each response and recorded their answers separately without reference to each other or to the previous results. The average of the four readings, for asymmetrical responses, or the two observers' readings for symmetrical responses, were then used to prepare the graphical figures.

It became clear early in the course of the study that a record of the changes in the diameter of these responses was not, in itself, adequate to characterise their course. Frequently the diameter of the responses, having passed its peak value, remained unchanged for many days while depth of palpable induration rapidly declined. It became necessary, therefore, to include in the day-by-day observations of the progress of the responses, an estimate of the depth of induration present. This cannot be readily measured as it is, for example, in cattle, but means of obtaining an accurate measurement are being investigated. For the present purpose, a clinical impression of the depth on palpation has sufficed and three levels of induration have been recognised:

(*a*) " Definite "—there is a tense plaque of which the edges are usually easily defined.
(*b*) " Shallow "—there is unequivocal induration, but the plaque is less well defined than in (*a*), the actual depth is less, and the transition from indurated to normal skin is less abrupt,
(*c*) " Very shallow "—the affected area can just be felt to be raised above the surrounding skin.

No serious difference of opinion occurred between the pairs of observers over the placing of responses within this classification, except in the case of (*c*), where quite commonly one observer recorded " very shallow " and the other " no induration."

Graphical Representation

In order to show in a single curve changes in the induration of these responses, it is necessary to represent both the diameter and the depth of induration at any given time. In the accompanying figures, the diameter of the response is given by the *lower* edge of the curve and the depth of induration by the thickness of the line. Since the changes involved are continuous, it has been felt justifiable to simplify the figures by connecting the discontinuous measurements by a continuous line and similarly converting the step-wise

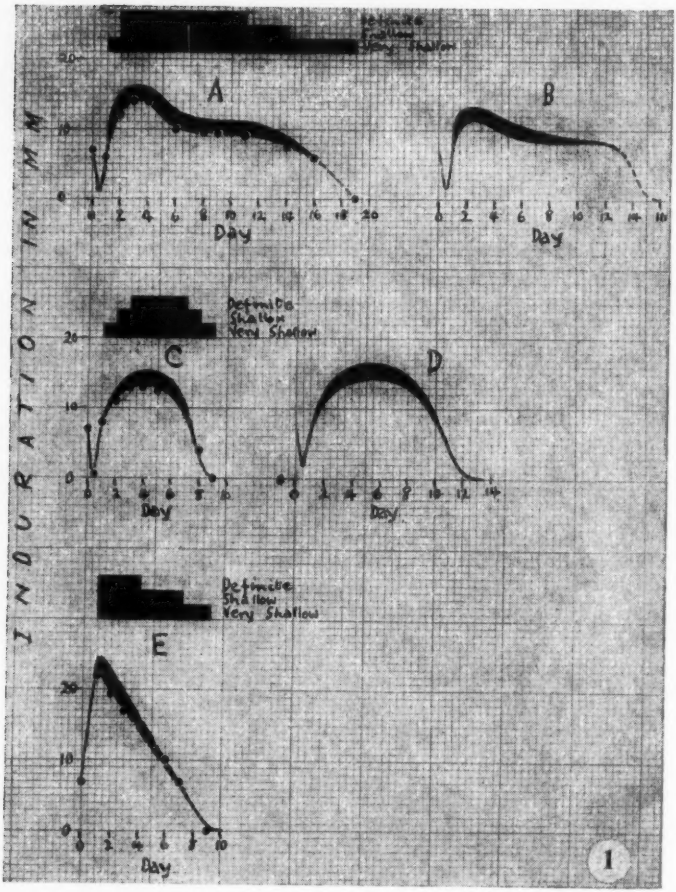

FIG. 1.—Examples of " normal " responses: A and B, Type I; C and D, Type II; E, Type III. A and C are taken from normal subjects, B from a case of bronchiectasis and D and E from cases of aspiration pneumonia. In curves A, C and E, the actual measurements are shown and the transition in depth of induration indicated by the block above the curve. Depth of induration is also indicated by the thickness of the line and the diameter of the response by the lower edge of the curve.

transition from " definite " to " shallow " to " very shallow " induration into a smooth curve. Curves A, C and E in Fig. 1 show the actual measurements and the derived smooth curves. In the remainder of the figures, the actual measurements have been omitted.

Results

Arrested Tuberculosis

Amongst the group not suffering from active tuberculosis, three kinds of reaction can be distinguished:

Type I. This is far and away the commonest type of response. Twenty-four hours after inoculation there may be no response or induration may already be developing. Usually the plaque arising from injection has completely or almost completely subsided after six hours and recognisable onset of reaction at this time is rare. The diameter of the response is maximal on the second or third day, subsequently declines a little, and then remains at this post-peak value for six to fifteen days during which time the depth of induration declines. Usually, " definite " induration remains for about the first two-thirds of the total life of the response, after which there is comparatively rapid transition to " very shallow " induration. The period of " shallow " induration may be very short, so that the induration from being easily palpable one day may be almost absent the next. The change from " very shallow " to " no induration " of course occurs, as it were, without change in diameter; this change is shown in the figures by a dotted line. Examples of this form of response in a normal person and a case of bronchiectasis are given in Fig. 1, Curves A and B.

Type II. This response is far less common than Type I and is characterised by its extreme symmetry about the point of maximum diameter and induration —both of which develop more slowly than in Type I, reaching their maximum about the fourth or fifth day. The decline is also more gradual in this type with a regular transition from " definite " to " shallow " to " very shallow " to " no induration. " Examples of this form of response in a normal person and a case of aspiration pneumonia are given in Fig. 1, Curves C and D.

Type III. This is the rarest of the three responses, but when seen is very characteristic. Induration is usually well developed after twenty-four hours and is commonly maximal at this time. The degree and diameter of induration are never maximal later than forty-eight hours after injection. From the peak value, the induration in terms of both diameter and depth falls linearly to zero. An example of this form of response in a case of aspiration pneumonia is given in Fig. 1, Curve E.

Active Tuberculosis

Many of the cases of active tuberculosis both treated and untreated gave responses indistinguishable from those described above, but in a significant number 28 (51·8 per cent.), responses were found which have, in this small series, not been encountered in the absence of active tuberculosis. These responses correspond closely in their essential form with those described above and are, for simplicity, regarded as derivatives of them. All differ from the responses from which they are regarded as being derived by the extreme transience of " definite " or " shallow " induration. Thus, in the Type I response of active tuberculosis, induration is again maximal in diameter at two to three days, but " definite " induration is frequently replaced by " shallow " after only twenty-four hours, and this " shallow " induration itself does not survive more than two days. In this way, although " very shallow " induration may persist for seven or eight days, induration of a greater degree than this lasts only for two or three days. Similarly, the form of the normal Type II and Type III responses is followed, but greater induration than " very shallow " lasts for not more than three days. Examples of these

responses in cases of active tuberculosis are shown in Fig. 2 and they are compared with the normal types to which they correspond in Fig. 3. In addition, besides the transience of the induration in depth, the whole response tends to be of shorter overall duration.

In a small number of cases, responses occurred in which, although the form and development of the reaction resembled closely those described, induration was replaced by an extremely diffuse soft swelling. The measurement of these lesions proved extremely unsatisfactory and there was unusually wide variation in each observer's day-by-day estimate. Three of these occurred in the treated tuberculous patients, two being of Type I and one of Type II. In all three palpable induration lasted for only one or two days. The fourth occurred in a case of bronchiectasis in which the soft diffuse swelling was replaced after forty-eight hours by shallow induration of normal type which in turn persisted for four days.

Primary Pleural Effusions

The majority of the small number of cases (22) so far examined showed " normal responses," but 7 (31·8 per cent.) showed the responses typical of active tuberculosis. No attempt has been made so far to determine whether these patients showed evidence of parenchymal disease.

In all three groups, arrested tuberculosis, active tuberculosis, and primary pleural effusion, Type I responses were the most common. For simplicity, the responses described under arrested tuberculosis are called " normal responses " and those described under active tuberculosis " tuberculous responses." Both groups are divided according to the scheme illustrated in Fig. 3 into Types I, II and III. Needless to say, not all reactions are so well defined as those illustrated. In some " normal " reactions induration is " shallow " throughout but the normal pattern is preserved. In others, induration is well developed but does not last as long as those illustrated. For purposes of classification, therefore, it is necessary to define limits for each type of response. A " tuberculous " response is one in which " definite " or " shallow " induration lasts for three days or less. A " normal " response is one in which " definite " or " shallow " induration lasts for four days or more.

The overall results for all groups are summarised in Table II.

TABLE II.—NUMBERS OF PATIENTS IN THE THREE GROUPS SHOWING " NORMAL " AND " TUBERCULOUS " RESPONSES

	" *Normal* "			" *Tuberculous* "			*Total*
	I	*II*	*III*	*I*	*II*	*III*	
Active tuberculosis untreated	6	1	1	5	2	1	16
Active tuberculosis treated	15	3	0	18	1	1	38
Arrested tuberculosis ..	50	4	2	0	0	0	56
Pleural effusion	13	2	0	4	2	1	22
Total	84	10	3	27	5	3	132

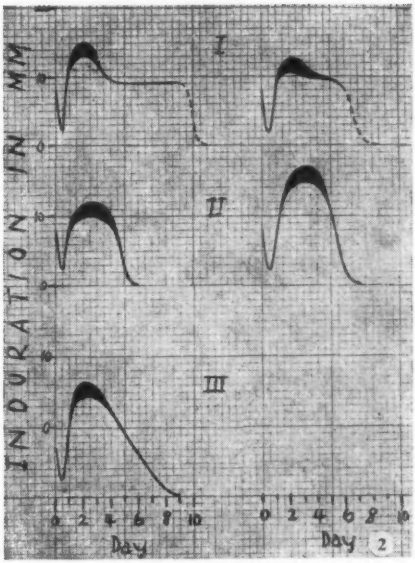

FIG. 2.—Examples of " tuberculous " responses taken from cases of active tuberculosis. Depth of induration is represented by the thickness of the line and diameter by the lower edge of the curve.

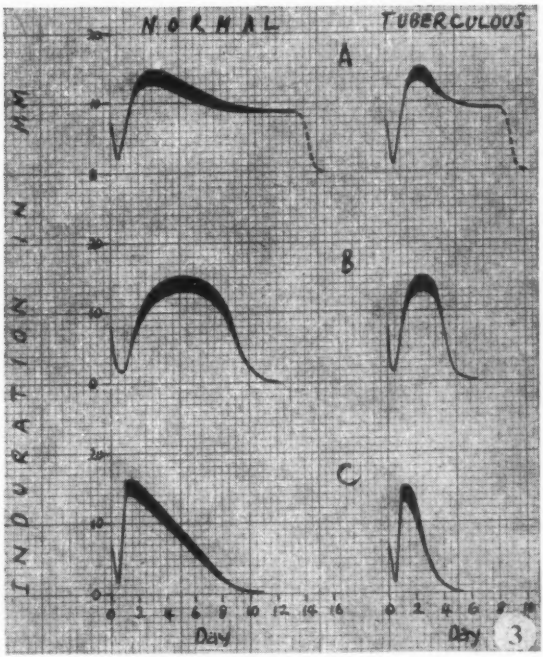

FIG. 3.—Comparison of the "normal " and " tuberculous " variants of the three types of response. Depth of induration is shown by the thickness of the line and diameter by the lower edge of the curve.

Erythema

The appearance of erythema in relation to these responses has been extremely variable. In some cases, well-marked induration has been associated with little or no erythema at any stage. Where erythema has been a feature of the reaction, it has usually rapidly increased in the first few days after injection and then equally rapidly declined, the peak usually overlying that of the induration (Fig. 4). In declining, the outlying erythema usually disappeared in a few days, but the indurated area remained red throughout

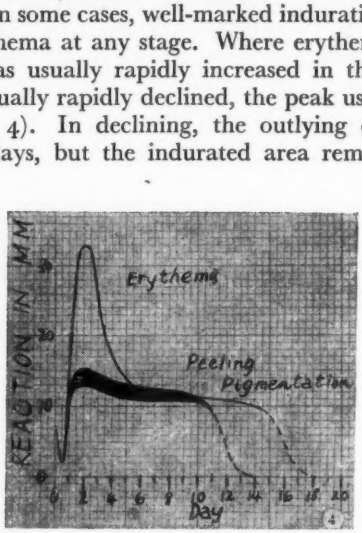

FIG. 4.—Relation of erythema to a typical Type I response. Depth of induration is represented by the thickness and diameter by the lower edge of the lower curve. Diameter of erythema is shown by the upper line marked "erythema." Peeling and pigmentation often appear at about the times marked on the graph.

its existence, and not infrequently erythema, later replaced by pigmentation and/or peeling, long outlasted induration. The erythematous area varied from involving the greater part of the width of the forearm to being just greater, when maximal, than the area of induration. Perhaps because the variation is so wide, no convincing difference in the behaviour of the erythematous response in the three types, or between the "normal" and "tuberculous" responses, has been demonstrated. If there is a difference, it appears to be that in certain tuberculous subjects erythema is remarkably persistent, but this may be falsely emphasised by the extreme transience of the induration in these cases. In four cases of treated active tuberculosis (two with healing miliary disease and two with healing localised lesions) erythema was the only response to the intradermal inoculation of 100 T.U.

Discussion

It has been shown that while many cases of clinically active tuberculosis show cutaneous responses to Old Tuberculin indistinguishable from those seen in subjects with evidence only of arrested disease, a significant number of cases with active parenchymatous disease or primary pleural effusion show a particular modification of the normal response not so far encountered in the absence of active tuberculosis.

A word is required regarding the strength of Old Tuberculin used in eliciting the response, and the magnitude of the reaction. If, for example, all the " tuberculous " responses were elicited by a dilution of Old Tuberculin of 1 : 10,000 and all the " normal " responses by 1 : 100, or *vice versa*, the difference could easily be a difference of dose response. Similarly, the " normal " responses might all follow large reactions and the " tuberculous " responses small reactions. The distribution of positive responses to various strengths and their average sizes in the two groups are given in Tables III and IV. It is

TABLE III.—NUMBER OF PATIENTS WITH " NORMAL " AND " TUBERCULOUS " RESPONSES AT VARIOUS DILUTIONS

	" Normal "		*" Tuberculous "*	
	Number	*Percentage*	*Number*	*Percentage*
Positive at a dilution of:				
1 : 10,000	50	51·5	5	14·3
1 : 1,000	43	44·4	27	77·1
1 : 100	4	4·1	3	8·6
Total	97	100·0	35	100·0

TABLE IV.—NUMBER OF PATIENTS WITH " NORMAL " AND " TUBERCULOUS " RESPONSES SHOWING INDURATION OF THE FOLLOWING MAXIMAL SIZES

	" Normal "		*" Tuberculous "*	
	Number	*Percentage*	*Number*	*Percentage*
Maximal size in mm.:				
17-22	5	5·2	0	0
14-16	23	23·7	7	20·0
11-13	34	35·0	16	45·7
6-10	35	36·1	12	34·3
Total	97	100·0	35	100·0

seen that there is a difference between them in the dose required to elicit a certain response. This difference, however, is unlikely to account for the change in reaction described, since there are clearly a large number of normal and abnormal responses in the same dose range and of the same size. The difference of level of response and type of reaction are evidently related, therefore, but not causally; there is a collateral rather than a dependent relationship. It appears that in the group showing the " tuberculous " response there is, compared with the " normal " group, both a decreased sensitivity to tuberculin, in that a greater stimulus is required to elicit a certain arbitrary reaction, and an attenuated response even when that reaction occurs. Such a change must be regarded as a step on the road towards " de-sensitisation," a modification in response to an antigen which is usually associated with repeated stimulation. Since care has been taken to exclude from the series

recently tuberculin-tested patients, it is tempting to think, if the same mechanism obtains, that there is intrinsic antigenic stimulation of which an active pulmonary lesion is an obvious source.

It would be expected, if any kind of autogenous de-sensitisation is occurring in active disease, that some patients would show a fully developed state of non-reaction. Amongst the patients with active disease tested in the present series, 4 had a negative Mantoux reaction in that they failed to produce induration on testing with 100 T.U. Two of these patients were suffering from healing miliary disease, but two had healing local lesions. Other workers (for example, James, 1950) have reported negative Mantoux reactions in active tuberculosis in the absence of the previously described causes which are reviewed by Mascher (1951) in a paper in which he describes 11 anergic cases in which the usual factors were not operative. It is certainly true that some young adults with localised active disease, whose general condition is good, may fail to react with induration to intradermal tuberculin.

Opinion in the literature regarding the effect of treatment with anti-tuberculous substances on the cutaneous reaction to tuberculin, even if man alone is considered, is, to say the least, widely divided. Many, especially Italian workers (for example Oricchio, 1950; Pinetti, 1950), claim that tuberculin sensitivity is increased by treatment, as does Turner (1953), while others (for example Leitner, Wetterwald and Beutl, 1951) claim that it is reduced. Despite widespread recognition of the importance of techniques and their standardisation, however, the variety of material and methods is so great that few of the published studies are directly comparable. In the present series, there is no difference in the percentage of cases showing the " tuberculous " response between the treated and untreated groups.

In suggesting again a possible relation between skin reactions and pulmonary lesions, it is important to emphasise that this does not mean that the reaction to tuberculin of the lungs at the site of the lesion or elsewhere, could it be measured, would necessarily be the *same* as that of the skin. It has been known for a long time (von Pirquet, 1907) that repetition of tuberculin testing, even with very small doses of antigen, may profoundly modify the response and that the level of sensitivity of the skin may spontaneously fluctuate considerably when followed for long periods (Forbes, 1938; Howe, 1938). The striking feature of the skin's response to tuberculin, in fact, is its lability. There is no evidence to suggest that this lability is shared by the rest of the body tissues in general or the lungs in particular, and there is some difficulty, therefore, when the level of skin sensitivity can be so easily altered in fixing the level which corresponds with that of tissues suffering from or liable to active disease.

Although the level and even nature of sensitivity of different tissues may not be the same, however, there may still be some definite, and perhaps reciprocal, relationship between them. It is even possible that the skin by its very lability, by its being demonstrably affected by very small stimuli, may indicate changes not recognisable by other means. Having said this much about marked changes in skin response after small antigenic stimuli, the final difficulty of the present work must be discussed. The majority of those showing the " tuberculous " response received two antigenic stimuli, while the majority of those showing the " normal " response received only one. It can be shown

that in certain circumstances a small dose of tuberculin of the order given in these cases can, after a very short interval, not only alter the level of sensitivity but alter it in precisely this kind of way (O'Grady, to be published). The possibility that this is the mechanism in these cases will be discussed fully elsewhere. At present, it suffices to say (*a*) that a large number of " normal " responses occurred after exactly the same stimulus and (*b*) that even if the immediate antigenic stimulus is derived from a previous tuberculin test the abnormal response is restricted to those with active tuberculosis.

Whatever the relationship between skin and lesion may prove to be, even in so small a series it is difficult to avoid the conclusion that a definite significance must attach to a change so absolutely related to demonstrable activity.

Summary

1. Three types of Mantoux reaction pattern based on estimates of diameter and depth of induration are described.

2. A specific modification of the normal patterns, characterised by extreme transience of induration, was seen in 51·8 per cent. of the cases of active pulmonary tuberculosis and 31·8 per cent. of the cases of primary pleural effusion examined.

This change has not so far been encountered in any patient not suffering from active tuberculosis.

3. The possible significance and mechanism of this change are discussed.

I am greatly indebted to Captain Anton Tabone, R.A.M.C., Sgt. A. O. Pawelski, Sgt. K. Hargreaves, Cpl. A. Congrave and Cpl. N. F. Bayley who, from time to time, have filled the essential and unrewarding rôle of " a second observer."

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PAINFUL INJECTIONS IN STREPTOMYCIN TREATMENT

A TRIAL OF FIVE SOLUTIONS OF STREPTOMYCIN SULPHATE

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Since 1952, when it was shown that injections of streptomycine sulphate caused less pain than injections using the calcium chloride complex, the former salt has been in routine use in this hospital (McLeod and Somner, 1952). Several pharmaceutical firms in this country have produced stabilised solutions of streptomycin sulphate, in order to reduce the risk of sensitivity in streptomycin handlers, and the time spent in administering the solutions.

Stabilised solutions have recently been used in this hospital and complaints of painful injections have become more frequent. It was therefore decided to determine whether intramuscular injections of stabilised solutions of streptomycin sulphate were more painful than those using the unstabilised streptomycin sulphate. This paper describes the results obtained.

Material and Methods

Five different preparations of streptomycin sulphate were used.

(1) Control solution: Streptomycin sulphate (Glaxo). 1 g. in 4 ml., freshly prepared, containing no stabilising agents or preservative—Solution C.
(2) Streptomycin sulphate (Boots) 1 g. in 2 ml., containing not more than 5 per cent. buffering and stabilising agents, and 0·5 per cent. phenol as preservative—Solution B.
(3) Streptomycin sulphate "Streptaquaine" (The Distillers Co. (Biochemicals) Ltd.) 1 g. in 4 ml. containing not more than 0·8 per cent. stabilising agents and not more than 0·5 per cent. phenol as preservative—Solution D.
(4) Streptomycin sulphate "Strepolin" 25 per cent. (Glaxo) 1 g. in 4 ml. containing 1 per cent. stabilising agents and 0·5 per cent. phenol as preservative—Solution G1.
(5) Streptomycin sulphate (Glaxo) 1 g. in 4 ml. containing 3 per cent. stabilising agents and 0·5 per cent. phenol as preservative—Solution G2.

Ten female patients whose ages ranged from 16 to 48 years were included in the trial. All were volunteers and most of them had complained spontaneously of painful injections.

Each patient received five injections of each preparation, that is twenty-five injections in all. The days on which each drug was given were selected in a

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random manner. One of us gave all the injections and he was the only person who knew which preparation was being used. Each day the other investigated the pain reactions of each patient and neither observer nor patients knew which preparation had been given.

Pain was graded as " early pain " (occurring within ten minutes of injection) or " late pain " (beginning or persisting for more than ten minutes after injection). The degree of pain in each grade was recorded on a points system as follows:

0—no pain;
1—slight pain;
2—moderate pain;
3—severe pain.

Separate specially marked syringes were used for the different preparations. Solution B was supplied in " viule " form; " viules " are glass cartridges containing the streptomycin solution and are given by a " Mitrex " syringe, which is similar to a dental syringe.

A new needle, size 3 serum, 2 inches long, was used for each injection.

The injection technique was the same for all patients and the upper outer quadrant of the gluteal muscle was the site used.

Results

The degree of pain caused by each injection was recorded by points 0, 1, 2, 3 as described above and was analysed under three headings—early pain, late pain and peak pain; by peak pain is meant the highest pain score occurring at any time after injection. The total number of points scored in each group is shown in Table I. The figures contributing to these totals represent the total pain score for five injections of each drug given to each patient. The ratio of actual pain score to maximum possible pain score (150) is calculated and the standard error for each ratio.

There was no significant difference between solutions in the scores for either early or late pain, as the individual ratios did not differ by as much as two standard errors.

For the peak pain group, however, the ratio for solution C was significantly lower than that for solution G2, but did not differ significantly from the ratios of solution B, D and G1; that is to say, solution C caused significantly less pain than solution G2, but the apparent differences in the pain scores for solutions C, B, D, and G1 were not statistically significant. Nor was there any statistical difference between the pain scores of the stabilised solutions B, D, G1 and G2.

A further analysis of the numbers of injections causing pain in the periods early, late, and at any time after injection, was carried out in Table II.

The X^2 test was applied to determine whether any one solution gave significantly more painless injections than any other.

In the early period solution C gave significantly more painless injections than G2 ($P<\cdot01$) and G1 ($P<\cdot02$). Amongst the stabilised solutions there was no significant difference in the numbers of painless injections.

In the late period C again gave significantly more painless injections than solution G2 ($P<\cdot01$). Amongst the stabilised solutions, solution G1 was

TABLE 1.—PAIN EXPERIENCED* BY 10 PATIENTS AFTER 5 INJECTIONS OF 5 TYPES OF STREPTOMYCIN SULPHATE IN 3 CATEGORIES—EARLY, LATE AND PEAK

	Early pain (within 10 minutes)						*Late pain (after 10 minutes)*						*Peak pain (at any time)*					
	C	*B*	*D*	*G1*	*G2*	*Total all drugs*	*C*	*B*	*D*	*G1*	*G2*	*Total all drugs*	*C*	*B*	*D*	*G1*	*G2*	*Total all drugs*
Patient																		
1	4	7	8	6	8	33	1	0	0	0	0	1	5	7	8	6	8	34
2	0	5	4	5	4	18	0	6	5	2	4	17	0	7	5	5	5	22
3	0	0	2	0	0	2	0	0	6	2	3	11	0	0	8	2	3	13
4	5	1	3	3	3	15	2	1	0	1	5	9	5	2	3	3	5	18
5	6	3	4	7	6	26	2	4	6	6	3	21	6	6	8	9	7	36
6	4	9	3	8	10	34	6	9	6	2	11	34	6	9	7	8	12	42
7	2	2	6	2	11	23	1	0	3	0	6	10	3	2	9	2	11	27
8	2	3	8	5	8	26	0	4	7	2	5	18	2	5	8	5	8	28
9	3	8	6	6	6	29	2	3	4	1	3	13	3	8	6	6	6	29
10	3	7	2	3	6	21	0	1	0	0	1	2	3	7	2	3	7	22
Total all patients ..	29	45	46	45	62	227	14	28	37	16	41	136	33	53	64	49	72	271
Ratio of actual pain score Maximum pain score (150)	·193	·300	·307	·300	·413		·093	·187	·247	·107	·273		·220	·353	·427	·327	·480	
Standard error ± ..	·0558	·0648	·0652	·0648	·0676		·0411	·0551	·0610	·0437	·0630		·0586	·0676	·0699	·0663	·0707	

* For each injection pain scores ranged from 0 to 3 (see text).

TABLE 2.—THE DISTRIBUTION OF PAINFUL INJECTIONS CAUSED BY 5 PREPARATIONS OF STREPTOMYCIN SULPHATE

	Early period					*Late period*					*Period at any time after injection*				
	C	*B*	*D*	*G1*	*G2*	*C*	*B*	*D*	*G1*	*G2*	*C*	*B*	*D*	*G1*	*G2*
Total No. of injections with severe pain ..	1	4	5	1	8	0	3	7	2	4	1	5	9	2	8
" " " " moderate pain	6	8	6	10	9	5	5	6	2	7	7	9	10	11	12
" " " " slight pain ..	14	17	19	22	20	4	9	4	6	15	16	20	17	21	24
" " " without pain ..	29	21	20	17	13	41	33	33	40	24	26	16	14	16	6

Early period within 10 minutes of injection.
Late period 10 minutes or more after injection.

C=Streptomycin sulphate (Glaxo) 1 g. in 4 ml. Control solution. Freshly prepared. No stabilising agent or preservative.

B=Streptomycin sulphate (Boots) 1 g. in 2 ml. Not more than 5 per cent. buffering and stabilising agents. 0·5 per cent. phenol as preservative.

D=Streptomycin sulphate "Streptaquaine" (Distillers) 1 g. in 4 ml. Not more than 0·8 per cent. stabilising agents. Not more than 0·5 per cent. phenol as preservative.

G1=Streptomycin sulphate "Strepolin 25 per cent." (Glaxo) 1 g. in 4 ml. 1 per cent. stabilising agents. 0·5 per cent. phenol as preservative.

G2=Streptomycin sulphate (Glaxo) 1 g. in 4 ml. 3 per cent. stabilising agents. 0·5 per cent. phenol as preservative.

significantly better than solution G2 ($P<\cdot01$), but the differences between G1, B and D were not significant.

In the period at any time after injection solution C was significantly better than any of the stabilised solutions: G2 ($P<\cdot01$), D ($P<\cdot02$), B ($P<\cdot05$), G1 ($P<\cdot05$).

Amongst the stabilised solutions, B, D and G1 were significantly better than solution G2: G1 ($P<\cdot02$), B ($P<\cdot02$), D ($P<\cdot05$).

Discussion

Recently Thomas and Penrhyn Jones investigated the pain occasioned by four different types of stabilised streptomycin (supplied by a single commercial firm) given to twenty patients. They found that " no patient complained of any unusual pain throughout the course with any of the four preparations."

As " unusual pain " is not defined it is difficult to know what degree of pain was regarded as being beyond the normal limits, but it is probable that no severe pain was caused.

We thought it easier to obtain a comparison between the solutions to be investigated by using a standardised technique operated at the same time each day by one person, and inviting the patients to grade and report their sensations to another whose enquiries were also made at a standard time daily, the patient and the second observer having no knowledge of which solution had been given. This was an attempt to assess lesser degrees of pain which might be of some importance to a patient receiving streptomycin for long periods.

Conclusion and Summary

The evidence presented in this enquiry shows that there was no significant difference in the amounts of early pain or late pain caused by any of the five drugs used. But if a comparison is made of the solutions in the peak pain group, solution C caused significantly less pain than G2 only. Amongst the four stabilised solutions there was no significant difference in the amount of pain caused by any, though G2 caused the most pain in all groups.

When the distribution of painless injections for the early period is studied, unstabilised streptomycin solution C was significantly less painful than two of the stabilised preparations G2 and G1, but between the stabilised preparations themselves there was no difference.

In the late period unstabilised streptomycin solution C was significantly less painful than only one of the stabilised preparations, G2, and between the stabilised preparations themselves G1 was significantly less painful than G2 but not less painful than B or D.

Analysing pain occurring at any time after injection, the unstabilised streptomycin solution C was yet again significantly less painful than any of the stabilised solutions. Among the stabilised solutions, B, D and G1 were significantly and almost equally less painful than G2.

Acknowledgment is made to Professor John Crofton, who suggested that this trial be carried out, for his advice and criticism of the paper, and to Dr. Lilli Stein of the Department

of Social Medicine and Public Health, who kindly gave us statistical advice. Our thanks are due to the patients for their willing co-operation. The streptomycin solutions and needles were supplied by Glaxo Laboratories Ltd., The Distillers Co. (Biochemicals) Ltd., and Boots Pure Drug Co. Ltd., who also provided the Mitrex syringe.

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DIRECT TRACHEAL LAVAGE FOR RAPID RECOVERY OF *MYCOBACTERIUM TUBERCULOSIS* FROM THE RESPIRATORY TRACT

By J. Spencer Jones

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Gastric lavage and laryngeal swabbing are the commonly accepted supplementary methods for recovering mycobacteria in cases of pulmonary tuberculosis. Little consideration has been given to tracheal lavage. Here further evidence is presented indicating the value of using this method and a simple, rapid technique is described.

General Considerations

The problem of the patient with pulmonary tuberculosis, who is unable to expectorate sputum for microscopy and culture, merits closer consideration. It would seem that, since the introduction of chemotherapy for tuberculosis, two types of failure of clinical judgment have resulted—both attributable to the anticipated end result of " sterilisation " of the sputum. On the one hand equivocal (but sometimes clear cut) tomographic evidence of cavitation has resulted in the resection of lesions which later prove to be solid (Maycock *et al.*, 1955). Without the confusing effect of chemotherapy in such cases a negative sputum could be taken as reliable evidence against cavitation. On the other hand, equivocal tomographic evidence has led to expectant treatment and subsequent relapse. In this connection Farquharson (1952), using data derived from a single hospital and clinic, has commented: " Already more people discharged in 1950 have relapsed than people discharged in 1947," going on to incriminate the impermanent effects of chemotherapy.

Clearly more and better information about the sputum during the first two months after chemotherapy might help. One is reminded of the words of Armand Delille (1927) when he first evaluated gastric lavage in adult cases of pulmonary tuberculosis: " . . . All available methods of study should be applied in the search for *M. tuberculosis*."

Supervising treated cases of pulmonary tuberculosis has always given surprises and chemotherapy has not changed this. Among the precautions frequently observed are monthly requests for examination of sputum specimens on three consecutive mornings. Ordering perhaps eighteen examinations in six months voices mistrust. Alternatively, in the absence of sputum, gastric lavage or two laryngeal swabs are sent for bacterial culture. The mind of the patient and physician alike seem resistant to the frequent employment of these latter measures and it is perhaps strange that they have not been superseded by tracheal lavage, which appears to be more sensitive.

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Tracheal Lavage

De Abreu described this method in 1944, under the name of " pulmonary lavage." Its development is so logical that it is surprising that it had not evolved before. De Abreu's method was to cleanse the mouth, anæsthetise the tonsillar plicæ and pharynx with 1-2 ml. of 0·5 per cent. of novotutocaine and allow a further 1-2 ml. of anæsthetic to be inhaled. Finally, 5-10 ml. of saline was injected through the open larynx and the resultant expectorated material was examined for *M. tuberculosis*.

In 1946 de Abreu reported 313 complete lavages and in 18 patients he compared the findings with those of gastric lavage. Of this number 8 proved positive by the new method and only 1 by gastric lavage.

Despite his suggestive findings, little interest was shown in this country. In the United States, Wardrip *et al.* (1949) stated that, in 111 patients, gastric lavage found no mycobacteria which were not recovered by tracheal lavage. In Britain, Lees *et al.* (1955) have recently compared the two methods on 144 patients and find that tracheal lavage gives nearly twice as many positive results as gastric lavage.

The technique advocated by de Abreu and followed by other workers, including Wardrip and Lees, may not have proved popular because of these objections:

(i) There is an explosive cough through the open larynx, in the direction of the operator.

(ii) Possible hazard from surface anæsthetics exists, both regarding toxicity and subsequent choking. Both these risks would be magnified in dealing with large numbers.

(iii) Natural reluctance of physicians to take upon themselves time-consuming duties which, in the case of gastric lavage, have previously been attended to by trained nurses.

Present Investigation

The earlier work of Clark *et al.* (1945) and Forbes *et al.* (1948) had shown that laryngeal swabbing was inferior to gastric lavage.

Because the sensitivity of tracheal lavage seemed greater than that of gastric lavage, and because Chaves (1953) had recently reported that two laryngeal swabs were only 72 per cent. as effective as a single gastric lavage in a series of 267 positive cultures, it was decided to use an alternative technique for tracheal lavage in the hope of finding a quicker and simpler method of obtaining reliable sputum data.

The method was applied to patients, unable to expectorate sputum, who were having gastric lavage for the recovery of *M. tuberculosis* in the normal way. After gastric lavage had been carried out by the nursing staff, tracheal lavage was done within a few minutes by the technique described below. In this way a further opportunity to compare the sensitivity of the two methods was available.

Technique

The patient lies on the examination couch with the neck extended on the pillow and a sputum container is placed in the hand. A Record syringe fitted with No. 1 needle and containing 5 ml. of sterile normal saline is at hand. While a simple explanation is given, the cricoid cartilage is palpated and the skin sterilised. After a warning of pressure, the needle is inserted through the space inferior to the cricoid cartilage. On withdrawing the plunger, air is obtained, indicating tracheal puncture. The patient is then told to expect a desire to cough which must be suppressed during the period of the injection (about 2 seconds). The injection having been made, the patient is sat forward and away from the operator and instructed to expectorate into the container.

In this way 5 ml. or more of saline and saliva are obtained, in which float mucoid or purulent specks. The presence of these particles is an assurance that the specimen is satisfactory and they are seen in sputum-positive and sputum-negative cases.

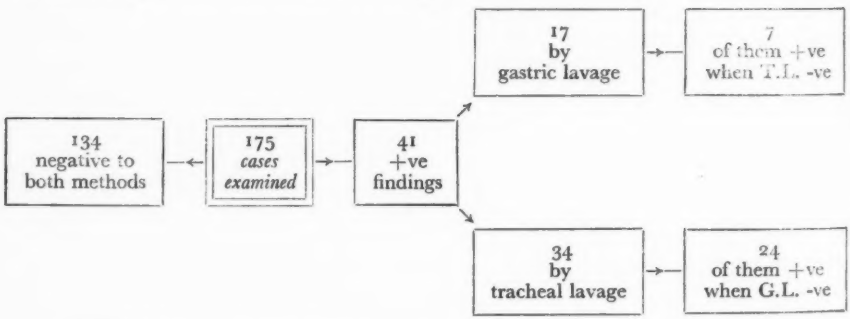
The time taken for the procedure, including explanation, is 40 seconds.

In apprehensive patients, the subcutaneous injection of a bubble of procaine 1 per cent. before the intratracheal injection, at the site of puncture, has a reassuring effect.

In the laboratory bronchial washings receive the same treatment as gastric washings with the omission of the neutralisation with sodium hydroxide. In this series gastric contents were neutralised within one hour of the lavage.

Results

There have been no complications and the procedure has been well tolerated by all but one patient, who said she had dysphagia during the day of the lavage. This was mild and insignificant.



Tracheal lavage found 83 per cent. and gastric lavage 41 per cent. of the total sputum-positive cases detected by both methods.

Of the 41 sputum-positive cases detected, 34 were found by tracheal lavage and of these 24 (59 per cent.) would have been missed if gastric lavage alone had been the only method employed. Gastric lavage compared unfavourably but did uncover 7 sputum-positive cases which were not found by tracheal lavage.

If the number of positive results for gastric lavage is expressed as a percentage of the positive results obtained from tracheal lavage, the figure obtained is 50 per cent. This is very close to the figure of 53·9 per cent. calculated from the data of Lees *et al.*

Discussion

Our present methods of obtaining sputum, when the patient cannot expectorate, are not very efficient. Unused sputum specimen bottles lead to exhortation and thus to waste of the time of a laboratory technician, who must examine any promising material offered. After further delay, gastric lavage is ordered, entailing the arrangement of an appointment and expenditure of the time of a trained nurse.

Although it cannot be said that pulmonary tuberculosis is a disease which will not allow of some delay in assessment, there can be no doubt that this is undesirable and so is misuse of laboratory and nursing staff. The advantages of determining whether or not sputum is available and proceeding at once to some investigation which can be carried out during the same visit seem clear. For this reason laryngeal swabbing has been adopted at some centres, but universal acceptance is lacking because of its lower sensitivity and perhaps also because of the risk of gagging and coughing in the direction of the operator.

Tracheal lavage, using the manœuvre described, offers definite advantages. It is more sensitive than other methods and is not time consuming. It is the practice in this area to apply tracheal lavage to all patients who need positive action in obtaining sputum data. By this means a specimen can be made available at the end of a consultation and questions about the disposal of newly diagnosed cases of pulmonary tuberculosis can sometimes be answered in twenty-four hours.

Further, when uncertainty exists about the status of a patient who has had chemotherapy for previously sputum-positive disease, tracheal lavage at each attendance is rational, quick and safe. In practice there is always hesitation about asking nursing staff to undertake the number of gastric lavages which would be required for adequate supervision of cases of this kind, apart from the feeling of inconveniencing the patient.

Summary

Sputum must be regularly examined if patients with pulmonary tuberculosis are to have proper supervision. This is especially true when recent chemotherapy may mask the picture.

Since tracheal lavage (" pulmonary lavage," " bronchial lavage ") is more sensitive than other methods of obtaining *M. tuberculosis* from patients unable to expectorate, it seems that it could be more widely used. In this series, tracheal lavage produced exactly twice as many positive sputum cultures as were obtained from gastric washings.

A quick technique for intratracheal injection, with the larynx closed, is described, which it is believed overcomes objections to the original technique of de Abreu.

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THE TREATMENT OF TUBERCULOUS LUNG CAVITIES BY CONTINUOUS INTRAPULMONARY DRIP

A PRELIMINARY REPORT

By D. J. M. Jenkin

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Introduction

A PRELIMINARY report has been published on a method of intracavitary injection in the treatment of pulmonary tuberculosis (Jenkin, 1953). At the present time an assessment of this method is in progress, and is based on an average of three years' follow-up of approximately fifty cases.

This assessment has confirmed earlier impressions that not all tuberculous cavities are suitable for treatment by this method. Such cavities are those with a mean diameter of more than 5 cm., most of those situated in the middle or lower lobes, acute or thin-walled cavities and cavities containing excessive amounts of pus or caseous material.

The reason that such cavities are unsuitable for this method of treatment is to be found in the nature of the medium itself. The hydrogenated ground-nut oil mixed with antibiotics, once injected into the lung cavity, becomes a solid, inert bulk of material. Under adverse circumstances this appears to act purely as a foreign body within an acute abscess cavity. The communicating bronchus becomes occluded, and any further drainage of accumulated pus is prevented. This is contrary to all surgical principles.

The unsuitability of such cavities was recognised very early in the course of this research. By insertion of a small-bore polythene tube and daily injection of antibiotics into the cavity, an attempt was made to prepare it for later treatment by injection of the mixed ground-nut oil and antibiotic medium. This method, already described in the article referred to above, has led to the development of continuous intrapulmonary drip for the treatment of tuberculous lung cavities.

The Method of Continuous Intrapulmonary Drip

Indication

Any residual tuberculous cavity in a patient who has had prolonged medical treatment and whose sputum remains positive.

Contraindications

Inaccessibility of the cavity to intubation.

A free pleural space.

(*Received for publication October* 4, 1955.)

Pleurodesis

Various methods for the artificial induction of an acute pleuritis and pleural symphysis have been discussed (Jenkin, 1953). More recently the author reverted to the use of talcum powder in conjunction with heavy sedation and intrapleural Xylocaine.

The use of a 25 per cent. suspension of kaolin powder has been described by Maxwell (1954). This has been tried in the form of an emulsion with preliminary pleural anæsthesia with Xylocaine. To date the latter method has proved the most satisfactory in inducing pleurodesis with the minimum of pain and reaction.

Cavity Intubation

Under sedation and local anæsthesia, using a suitable trochar and cannula, a rubber catheter of suitable size is inserted as far as possible into the cavity to be treated. Whenever possible the anterior approach should be used, and the operation is best performed under radiological control. A safety-pin through the catheter and strapped to the chest will keep the catheter securely in position.

The catheter is connected to underwater drainage and left for ten days. During this time the sinus granulates and the risk of surgical emphysema is thus reduced. At the time of operation or during the next ten days material aspirated from the cavity is cultured for secondary infective organisms. These are identified and their sensitivity to various antibiotics is ascertained by routine sensitivity tests. From the eighth day onward the patient's twenty-four-hour sputum output is measured and recorded.

Continuous Intrapulmonary Drip

The apparatus required is simple and easily assembled (Fig. 1). Two glass bottles with wide mouths (A and B), and of approximately 200 ml. capacity, are fitted with rubber stoppers. Each stopper is pierced by two glass tubes. One extends almost to the bottom of the bottle, the other terminates at the level of the stopper.

One of these bottles (A) contains the antibiotic solution and is inverted and suspended from a tripod transfusion stand. The shorter of the two glass tubes is connected by rubber tubing to a Laurie's Drop Regulator (C), then to one of the upper limbs of a Y-shaped glass union (D). The other limb of the union is connected to the longer glass tube of the second bottle (B). This bottle is suspended upright at a level not higher than the drop regulator. The vertical limb of the union is connected directly and in a straight line to the catheter leading to the cavity to be treated. The length of the latter connection should be as short as possible, and any kinking or looping of this tubing must be carefully avoided. A screw-action tubing clamp (E) is placed between the drop regulator and the Y-shaped union.

THE ANTIBIOTIC SOLUTION

This may be varied according to individual preference and the result of sensitivity tests.

The standard solution employed consists of 1,500 or 3,000 mg. of " Rimifon Roche " (INAH) in 60 or 120 ml. respectively, which is used to dissolve 5 g. streptomycin, 1,000,000 units of penicillin and 1 g. of terramycin. The preparations used must go into solution as a suspension is most undesirable. The prepared solution will not keep, and must be used on the same day.

After a light breakfast the patient is postured in a manner that places the cavity as near as possible to a dependent position in relation to the rest of the lung and to its communicating bronchus. Usually raising the foot of the bed is sufficient for upper lobe cavities, the prone position for dorsal lobe cavities with posterior intubation.

The drip is connected and regulated to run as slowly as possible. The total amount is expected to require eight hours, including occasional periods when the drip is shut off to give the patient a rest. Coughing soon commences, becomes severe, but should not be allowed to become too exhausting. In this case the drip is temporarily shut off. Sputum output increases considerably. This is measured, the amount of antibiotic solution run in is subtracted, and the resulting sputum output is recorded for each twenty-four hours.

The patient becomes febrile, usually by the end of the first day. This is due to liquefaction of material within the cavity, with dissemination and absorption of toxic products. Adequate antibiotic cover is administered parenterally or by mouth, the antibiotic of choice being selected from preliminary sensitivity tests on secondary organisms previously obtained from the cavity. One gramme streptomycin is given daily, together with maximum doses of INAH, over the earlier weeks of treatment by intrapulmonary drip, and between each treatment underwater drainage of the cavity is maintained.

If there is inclination to eat, the patient is given a light lunch and supper, and adequately sedated at night to obtain rest and recuperation. Depending on the condition of the patient and response to the drip, the procedure may be repeated at weekly or bi-weekly intervals. Initially the reaction is severe, and the drip may have to be discontinued after two or three hours. However, with each procedure the reaction becomes progressively less severe. Eventually there is no rise in temperature, little or no sputum output apart from the antibiotic solution, and coughing is less troublesome. Radiological deterioration may appear following the initial procedures. This is due to bronchial aspiration of infected material and toxic products, but clears on adequate antibiotic cover. Naturally the patient may lose weight, but this is soon regained after treatment.

It is necessary that the catheter in the chest be cleaned and replaced at frequent intervals. Occasionally it is necessary to insert a larger size. It is important that the catheter be inserted well into the cavity, otherwise, as the cavity closes the catheter tip leaves the cavity and the intervening sinus track may heal and the cavity become inaccessible to further treatment.

Case Illustrations

Two cases are described to illustrate the response to treatment by intrapulmonary drip.

The first case is that of a European male aged 27 years. For the last seven

years he has been receiving treatment for pulmonary tuberculosis which has had no effect on a large cavity in the apical segment of the right lower lobe.

Right pleurodesis was achieved by intrapleural instillation of 2 ml. 25 per cent. kaolin suspension in water (Maxwell, 1954), and on March 1, 1955, intubation of the cavity was carried out and connected to underwater drainage. On March 9 bi-weekly intrapulmonary drip into the cavity commenced.

The patient received a total of twelve intrapulmonary drips over a period of six weeks. By the end of the eighth week the cavity had disappeared completely and the tube had been withdrawn from the chest.

Chest X-ray in February 1955 before treatment shows the persistent cavity in the right mid-zone (Fig. 2). X-ray in May after treatment shows the cavity to have disappeared, and the presence of a notch in the upper border of the eighth rib posteriorly, due to pressure by the tube (Fig. 3). The patient's temperature chart during the first four weeks of treatment is illustrated in Fig. 4.

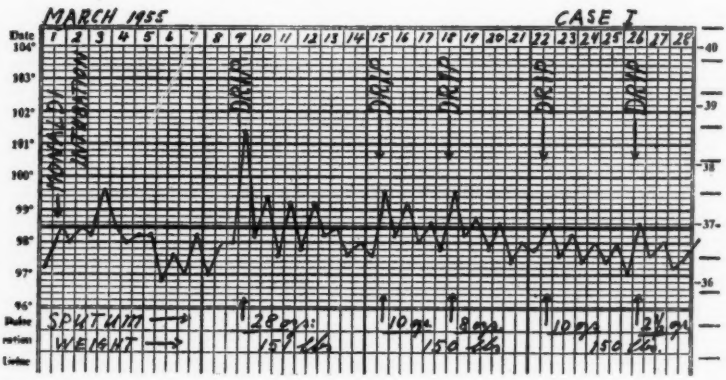

FIG. 4.

Clinically the patient has responded well after conclusion of this treatment. He is now symptomless, has no cough and produces no sputum whatsoever. Gastric lavage is necessary for routine tests for tubercle bacilli. These tests remain positive owing to the presence of a cavity in the apex of the right upper lobe, only obvious on tomography, and which is now undergoing similar treatment. The patient's weight, never higher than 155 lb. during the last three years, has now (August 1955) increased to 175 lb. from 151 lb. before treatment commenced.

The second case is that of a European female aged 26 years. She has been receiving treatment for pulmonary tuberculosis for the past five years and also suffers from rheumatoid arthritis, affecting the joints of the wrists and fingers. Tuberculous cavitation has been present in both upper lobes for the past four years, and has not responded to medical treatment.

Bilateral pleurodesis was achieved in 1953 after repeated intrapleural instillations of glucose-iodine solution. Both cavities were then treated by

PLATE X

Apparatus for continuous intra-pulmonary drip.

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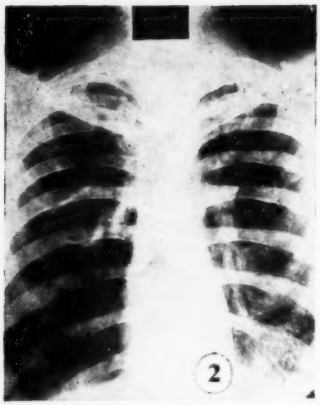

FIG. 2.—Chest X-ray, Feb. 1955, showing persistent cavity right mid-zone.

FIG. 3.—Chest X-ray after treatment sho resolution of cavity.

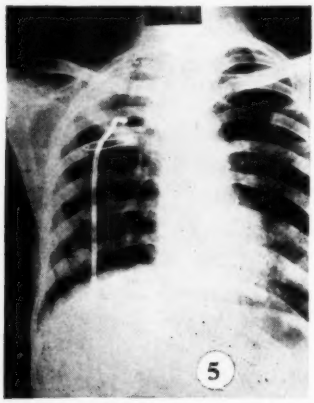

FIG. 5.—Chest X-ray showing drainage tube leading to right upper lobe cavity.

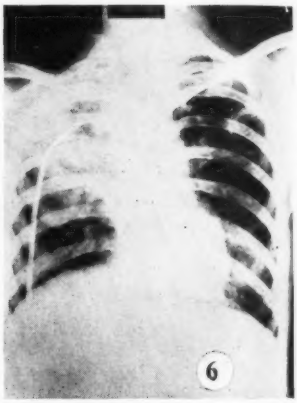

FIG. 6.—Chest X-ray a week after first intr pulmonary drip showing acute reaction fro bronchogenic spread.

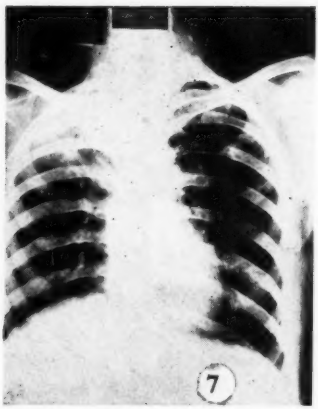

FIG. 7.—Chest X-ray 12 weeks later showing complete closure of cavity.

injection of hydrogenated ground-nut oil and antibiotics (Jenkin, 1953). Successful results following this treatment were only temporary, and after six months the medium became fragmented and coughed out of both cavities, and her sputum reverted to positive.

Intubation and underwater drainage of the right upper lobe cavity was carried out March 15, 1955, and treatment by intrapulmonary drip commenced on March 30. The patient received a total of eight drips over a period of thirteen weeks, at the end of which time the cavity had closed and the tube was withdrawn from the chest.

X-ray of this patient's chest on March 23 shows the drainage tube leading to the right upper lobe cavity, and a smaller cavity in the left upper lobe (Fig. 5). X-ray on April 5, one week after the first intrapulmonary drip, illustrates the acute reaction that occurred in this patient from bronchogenic spread throughout the right lung of disseminated toxic products following initial treatment of the cavity (Fig. 6).

X-ray of the chest twelve weeks later shows complete closure of the right upper lobe cavity (Fig. 7). Together with residual fibrosis there remains evidence only of the sinus track from which the tube was removed immediately beforehand, and a notch in the upper border of the second rib anteriorly. There is no evidence of the earlier bronchogenic spread, now completely resolved. The cavity in the left upper lobe remains to be similarly treated.

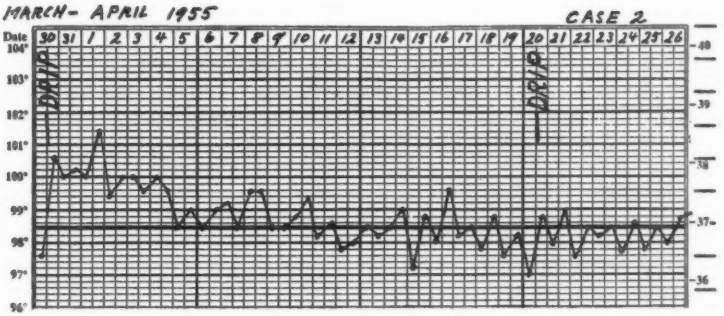

FIG. 8.

The patient's temperature chart during the first four weeks of treatment is illustrated in Fig. 8. Since the conclusion of treatment her clinical condition has shown marked improvement. She weighed 102 lb. in April before treatment commenced, and now (August 1955) weighs 113 lb., the most since her stay in hospital. Her sputum output now consists of scanty morning specimens only, and she has noticed marked alleviation of the pain and stiffness of her arthritic joints. Sputum conversion is anticipated after treatment of the left upper lobe cavity.

Discussion

Up to the present time treatment by intrapulmonary drip has been applied to eight patients. All are Europeans and all have two or more cavities to be treated. Complete cavity closure has been obtained in three patients. The remaining five are still undergoing treatment, but in each of these successful results are anticipated in that considerable reduction in cavity size and sputum output has already occurred. In every patient there remains a second or third cavity yet to be treated, therefore at this stage sputum conversion has not occurred to enhance the results of treatment.

Other than those already described, untoward effects of treatment have not occurred. Following this form of " medical curettage " of a tuberculous cavity, slight blood-staining of the sputum is to be expected, and apart from the necessity for reassuring the patient, is ignored.

The antibiotic solution used and the method of introducing it into the lung cavity are arbitrary, and may be varied according to individual preference. The method already described—that is, combining cavity drainage with intrapulmonary drip—has to date produced satisfactory and uncomplicated results.

In an earlier series the author's experience with small-bore polythene tubes was not satisfactory. The mechanical difficulties encountered with smaller or closing cavities offset any advantage of the polythene tube over the more flexible and versatile rubber catheter.

Summary

A method of treatment of tuberculous lung cavities is described. Antibiotics in solution are run into the cavity and, combined with cavity drainage, have brought about complete or partial cavity closure, reduction in sputum output and clinical improvement in eight patients so treated.

To Dr. B. A. Dormer, Medical Superintendent of King George V Hospital, Durban, whose patients were treated by the method described.

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PULMONARY TUBERCULOSIS SIMULATING BRONCHOGENIC CARCINOMA

By N. S. Dontas and J. G. Callanan

From the London Chest Hospital

Differential diagnosis between pulmonary tuberculosis and bronchogenic carcinoma is now more frequently necessary. There are two main reasons for this: (1) the increased awareness of the rising incidence of bronchial cancer, and (2) the growing number of male subjects who first develop tuberculosis in the fourth or fifth decades of life.

The occurrence of 14 cases where tuberculosis was confused with carcinoma in one surgical service within a few years prompts us to draw attention to certain points.

There have been previous reports on the differential diagnosis of pulmonary tuberculosis and bronchogenic carcinoma. Friedlander and Wolpaw (1940) presented 4 cases of chronic inflammatory lesions of a radiological type indistinguishable from carcinoma and impossible to diagnose even at operation. Thornton and Adams (1944) reported 23 cases of solitary circumscribed opacities and recommended thoracotomy as the surest method for establishing the diagnosis. Gottlieb and Shaslin (1948) had the same problem in 7 cases, but in none was thoracotomy undertaken. In all these bronchoscopy and biopsy were negative. They considered two to be pulmonary tuberculosis and the others various types of pneumonia and lung abscess. Kross (1950) mentioned one case in which a pneumonectomy was performed for what eventually was shown to be " tuberculoma " of the lung. Haight and Farris described a similar case. Shefts and Hentel (1950) had one lobectomy performed for presumed bronchogenic carcinoma, which proved, however, to be tuberculosis. Kergin (1952) described 8 cases of unilateral massive densities in the lung which clinically and radiologically appeared to be carcinoma, but which were, in fact, due to chronic pneumonitis. Three were found to be tuberculous and he suggested that the condition be called " silicotic lymphadenitis with obstructive pneumonitis."

Co-existence of tuberculosis and bronchogenic carcinoma is not uncommon. Shefts and Hentel (1950), Helm and Moon (1952), Ellman (1953), Sakula (1955) have described examples of the simultaneous occurrence of these conditions. The question of this combination presented four times in our series (cases No. 2, 9, 12, 13).

Clinical Features

There is no clinical pattern common to this group. Eleven of our patients were males over 40 years of age, and in some the abnormality was detected

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on mass radiography. In the majority there was a history of a chest illness characterised by cough, with or without sputum, and chest pain persisting for three to six months. Only two had slight hæmoptysis; weight loss was reported in seven; one man presented the problem of an unaltered mass in the left upper lobe after one year's continuous chemotherapy for proven tuberculosis. A positive tuberculous contact history was found twice. The association of a previous illness known sometimes to be related to pulmonary tuberculosis occurred on two occasions, namely homolateral spontaneous pneumothorax, and hæmoptysis from a primary tuberculous complex.

Radiological Aspects

In six of our cases there were solid homogeneous opacities, 4 cm. or more present: in two others this mass was accompanied by satellite shadows in the same lobe or adjacent lung. In only two there was evidence of central cavitation which posed the question of distinction between pulmonary tuberculosis and a breaking down carcinoma. One of these was known to have a positive sputum at the time of operation, and the other eventually became positive. Four of our cases had a clinical and radiological appearance of pneumonia confined to one lobe.

The anatomical position of a homogeneous mass in the lung is a useful pointer to establishing the correct diagnosis. The posterior segment of the upper lobe and the apical lower lobe segment are most often affected in tuberculosis. Ten of our patients had lesions on one or the other of these sites. The remainder showed pleurisegmental shadows, always involving posterior areas. It is known that bronchial carcinoma is sometimes associated with homolateral or contralateral metastases, but this is more often found at operation or autopsy than radiologically. A second kind of satellite shadow found in bronchogenic carcinoma, due to distal infarction (Hanbury, 1954), is unlikely to cause confusion.

Pathological Findings

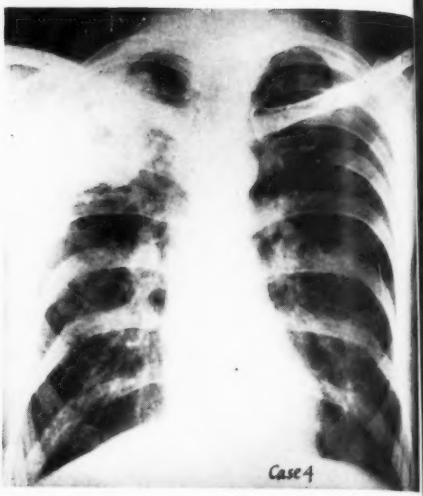
In all cases the pathological report on the resected specimens was fibrocaseous tuberculosis, usually without evidence of cavitation.

Management

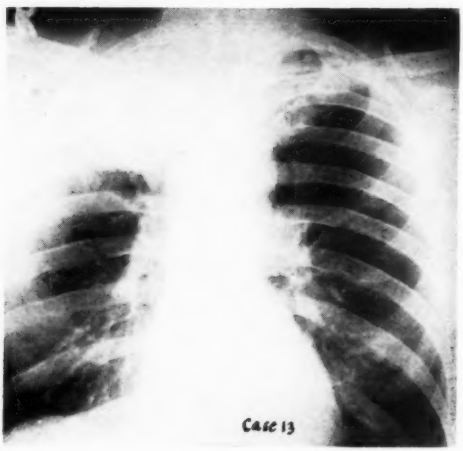
The investigation of any patient with these radiological findings should include bronchoscopy and sputum examination for tubercle bacilli and neoplastic cells. The likelihood of missing a carcinoma in the absence of a positive biopsy is small if six consecutive specimens of sputum are negative for malignant cells, provided that examination be made by a pathologist experienced in this technique (Jennings and Shaw, 1953). A positive report soon after bronchoscopy is of doubtful significance (case No. 12), even when microscopy of the lesion demonstrates the presence of metaplasia. The search may have to be continued for weeks (case No. 9) before a positive finding is obtained. Bronchoscopy was not helpful in our experience.

Thoracotomy will be necessary in most of these cases, and it will probably

CASE No. 1.—Male. Age 47. He had one year's general and chest symptoms with productive cough and positive sputum. He was treated with P.A.S. The X-ray showed solid opacity at the posterior segment of the upper lobe which remained unchanged for six months. The bronchoscopy was normal. He had a left upper lobectomy and the report confirmed a fibro-caseous non-cavitatory tuberculosis.



CASE No. 4.—Male. Age 47. He had persistent pleurisy and pneumonia for three months. His X-ray shows breaking down mass in the RUL. 7 cm. in diameter. Sputum negative for malignant cells and AFB. The bronchoscopy was normal. A right upper lobectomy was undertaken and the pathological report was confluent tuberculosis.



CASE No. 13.—Male. Age 52. He had pneumonia for 3 months and his X-ray shows a consolidated RUL. which remained unchanged after 3 months' drugs. Sputum was positive for AFB. The bronchoscopy was normal. He had a solid upper lobe which was resected and the report was "fibro-caseous tuberculosis with bronchiectasis and segment stenosis."

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be undertaken after a few weeks of antibiotic therapy. It may not, however, provide a solution. Apart from the question of site, the finding of calcified or adherent lymph nodes in the area adjoining the lesion, whilst favouring tuberculosis, will not entirely exclude the possibility of carcinoma, as Woodruff (1951) has shown.

It is in such cases that we have found a frozen section of a solitary tumour of assistance. This was done in case 6 and enabled us to exclude a malignant condition; an important fact in determining the extent of surgery necessary. It seems unlikely that it would be safe to perform this examination in cases with satellite lesions, and in such the extent of resection must be determined on the anatomical limits of the tumour mass.

In view of the above radiological and pathological facts we would in cases of doubt recommend a conservative rather than a radical procedure.

Summary

Fourteen cases of pulmonary tuberculosis simulating bronchogenic carcinoma are presented.

In 9 of the 14 cases all investigations prior to operation proved negative. In four cases the problem of simultaneous occurrence of bronchogenic carcinoma with pulmonary tuberculosis was considered an indication for operation.

The presence of sputum positive for AFB in radiologically solid homogeneous opacities in the lungs should suggest a firm diagnosis of pulmonary tuberculosis.

A diagnostic thoracotomy should be performed in this type of case and we recommend that frozen section be done at the time of operation. By this means the extent of resection may be reduced if malignancy can be excluded.

We wish to thank Mr. J. R. Belcher for his help and permission to record these patients.

(Table I appears on the two text pages following.)

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TABLE I.

No.	*Age*	*Sex*	*Clinical History*	*X-ray appearances*	*Sputum*		*Bronchoscopy*	*Operative findings*	*Pathology*
					A.F.B.	*Cells*			
1	47	M	1 year general and chest symptoms. Treated with PAS	Solid opacity posterior segment LUL 5 cm. diameter associated with other shadows. Opacity unchanged over 6 months	+	–	Normal	Atelectatic LUL. Nodular disease in the lingula	Fibro-caseous non-cavitatory tuberculosis.
2	48	M	14 months previously L. spontaneous pneumothorax. Symptom free. MMR finding. One brother died of carcinoma recently; one sister had pulmonary tuberculosis 3 years ago	Solid homogeneous opacity LUL, 4 cm. in diameter	–	–	Normal	Mass extended from posterior segment into lingula	Ditto
3	44	M	At age of 20 left pleurisy, cough and hæmoptysis and pain over 2 months. No abnormality on examination	Solid opacity in posterior segment RUL	–	–	Not done	No other disease found, but lumph nodes adherent to pulmonary artery	Ditto
4	47	M	Persistent pleurisy and pneumonia for 3 months	Breaking down mass in posterior segment 7 cm. in diameter	–	–	Normal	Rest of lung normal	Confluent tuberculosis confined to upper lobe.
5	62	M	Dyspnœa and chest pain for 5 weeks	Left parahilar mass 5 cm. in diameter in apex of lower lobe. Satellite shadows peripherally	–	–	Normal	Palpable disease in LUL, lingula and apex of LLL	Fibro-caseous tuberculosis.
6	43	M	Malaise, weight loss for one year, syphilis 1940. Father died of cancer 1946	Solid opacity apex R. lower lobe, extending peripherally. Radiological "scar" after 6 weeks' chemotherapy	+	–	Reddening of apical lower lobe bronchus	Not operated on	–

			of cancer 1946	Radiological "scar" after 6 weeks' chemotherapy			lobe bronchus		
7	29	F	No symptoms. Routine X-ray; rheumatoid arthritis	Mass in posterior segment LUL	−	−	Left bronchial tree reddened	Mass extended to periphery, with overlying thickened pleura. Mottled hilar lymph nodes. Rest of lung normal	Frozen section—fibro - caseous tuberculosis.
8	66	M	Lassitude, cough and sputum 6 months. Improved on penicillin	Solid RUL with hilar opacity. Old tuberculosis RLL and LMZ	−	−	Normal	Several other masses in RUL	Fibro-caseous tuberculosis.
9	50	M	Cough and sputum, dyspnœa, weight loss over 2 months. Wife has had pulmonary tuberculosis	4 cm. mass in RUL not homogeneous. Excentric cavitation. Apparent increase on serial films	+	−	Not done	Mass confined to UL	Fibro-caseous tuberculosis.
10	59	M	Cough and lethargy for 3 months	Solid opacity RUL. A blocked posterior segmental bronchus seen on bronchogram	−	−	Normal	Also a few nodules in anterior segment of UL	Fibro-caseous tuberculosis.
11	35	M	Cough and loss of weight for 3 months	In LUL pneumonic appearance without cavitation. Calcified lesion right apex	−	−	Blocked apico-posterior segmental orifice	Solid upper lobe. Rest of lung normal	Fibro-caseous tuberculosis.
12	56	M	Malaise, cough, weight loss 3 months. Pyrexia 101 F.	Consolidated RUL. Unaltered after 3 months' chemotherapy	+	+ on two tests, but after bronchoscopy	Normal	Solid upper lobe with scattered tubercles visible	Fibro-caseous tuberculosis associated with collapse. Metaplasia in bronchial epithelium.
13	52	M	Pneumonia for 8 weeks	Consolidated RUL. Unchanged after 3 months' drugs	+	−	Normal	Solid upper lobe	Fibro-caseous tuberculous bronchiectasis. Segmental stenosis.
14	37	M	No symptoms. Mother died of pulmonary tuberculosis 2 years ago	MMR. Posterior segment RUL 4 cm. opacity. Homogeneous	−	−	Normal	Solid lesion with overlying thickened pleura	Fibro-caseous tuberculosis calcifying in places.

TUBERCULOUS RHINITIS

REPORT OF A CASE

By I. Malcolm Farquharson and Douglas T. Kay

From the Ear, Nose and Throat Department, Royal Infirmary, Edinburgh, and the Department of Tuberculosis and Diseases of the Respiratory System, University of Edinburgh

Tuberculous infection of the nose is uncommon. When it does occur it is more frequently secondary to pulmonary disease. Twenty-eight unusual sites of primary tuberculous infection were described by Miller (1953), but the nose did not feature in that series. St. Clair Thomson (1948) mentioned that nasal tuberculosis in acute miliary disease has only twice been recorded.

We thought, therefore, it would be of interest to describe a case of tuberculosis of the nose we have recently seen.

In October 1954 a girl aged 12 was referred because blood had been found coating the lips and teeth, and lying in the right nostril. Her mother had died two years previously from pulmonary tuberculosis, and her father and her stepmother each had quiescent pulmonary tuberculosis and were under observation.

From earlier contact examination she was alleged to be tuberculin positive at the age of seven.

On examination she was generally of healthy appearance. The nasal septum was congested but free from any suspicious infiltration. Her gums were rather spongy, tonsils buried and congested, and the pharynx was healthy. She had a ridge of adenoids in her nasopharynx. The larynx was normal in both form and movement.

A radiograph of the chest revealed only a calcifying primary complex in the left upper lobe with some possible left hilar enlargement. No cavitation was found on tomography. The Mantoux test was positive to 1 in 10,000 Old Tuberculin.

Four weeks later, her general condition was still good but she complained of nasal obstruction. There was crusting inside the right nostril. Chest radiograph was unchanged.

A month later there was purulent rhinorrhœa, and examination of the nose showed pale pink discrete nodules spreading over the whole of the right side of the cartilaginous part of the septum; a similar infiltration was seen on the anterior part of the inferior turbinate bone on the right side. These pale pink discrete nodules were also seen involving the mucocutaneous junction of the left side of the septum. The turbinals were not involved on the left side of the nose. No ulceration was present, but there was a sticky mucoid discharge overlying these areas of infiltration. On the left side of the posterior pharyngeal

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wall discrete pinkish-coloured nodules were seen—one or two showing superficial ulceration.

Some blepharospasm was present and there was epiphora in the right eye, where a 2-mm. phlycten at the margin of the inferomedial quadrant of the cornea was seen.

Moderate rubbery enlargement of the lymph glands was now present in the right anterior deep cervical chain.

Nasal biopsy was positive for tuberculosis: the connective tissue underlying the squamous epithelium was heavily infiltrated with chronic inflammatory cells. One or two quite characteristic tubercles were present showing giant cells but no definite caseation.

Two cultures from nasal swabs taken were positive for tubercle bacilli which on both occasions proved sensitive to streptomycin, para-aminosalisylic acid (PAS) and isoniazid.

Treatment

Chemotherapy was commenced with streptomycin sulphate (1 g. on alternate days), PAS (10 g. daily) and isoniazid (0·2 g. daily), but after six weeks when the sensitivity reports were available, one of the drugs (streptomycin for convenience) was stopped and the PAS and isoniazid were continued.

Bed rest was prescribed only for the first month and thereafter she was progressively allowed up. Soft paraffin was applied to the nose; cortisone eye drops were used.

Progress

After six weeks' chemotherapy, nasal and laryngeal swabs were negative.

In three months only slight septal scarring remained. The phlyctenular keratitis had healed. Her general condition, which was only fair at the start of the illness, was now good and 12 lb. in weight was gained.

In six months the child appeared very well in all respects and was leading a normal life. PAS and isoniazid were being continued.

No pulmonary tuberculosis was found amongst her school contacts.

Discussion

It seems that this nasal infection was not a primary one, because it arose in the presence of an already calcified lung complex, and the tuberculin test was known to have been positive at an earlier age. Clinical and radiographic evidence did not suggest that the pulmonary lesion was active.

The patient's organisms were sensitive to streptomycin, PAS and isoniazid on two occasions, and it therefore did not appear likely that we were dealing with an exogenous infection from her mother, whose organisms were known to be resistant to streptomycin (resistance ratio 512), PAS (resistance ratio 266) and to isoniazid (growth on 5 mcg./ml.).

It was therefore tempting to speculate that the nasal infection had been a blood-borne one from an endogenous source of some duration. Further support to this supposition was lent by the bilateral distribution of the lesions

in the nasal cavity and the fact that the conchæ and the septum were affected equally. There was no history of trauma—for example to the septum—which might have constituted a portal of entry for exogenous infection such as from a handkerchief or finger nail.

The response to anti-tuberculous chemotherapy was rapid and satisfactory, in keeping with results achieved in treating tuberculosis affecting other mucous membranes.

In this case, in the presence of the proved tuberculous nasal disease there was little doubt about the pathogenicity of the tubercle bacilli found but it is perhaps well to recall that as early as 1910, Chapin stressed how important it was not to over-emphasise a chance finding of tubercle bacilli in the nose. Straus (1894) examined the nose in 29 healthy persons—orderlies, nurses and physicians working in tuberculosis wards—and recovered tubercle bacilli from 9. Cornet (1907) had found them in his own nose. Similar results had been reported by Möller (1899) and Bernheim (1905), but Le Noir and Camus (1908), on the other hand, had been unable to confirm such findings.

A brief analysis of the records of the Ear, Nose and Throat Department from 1944 to 1954 was undertaken and the results substantiated the rarity of tuberculous rhinitis. At this clinic only 34 cases were recorded out of approximately 88,500 patients. Thirty-two patients were female and two were male. They had been divided into the lupoid type (73 per cent.) and the acute tuberculous type (26 per cent.) One per cent. was in the form of a localised tuberculoma. All the cases had been diagnosed clinically, and histological confirmation of each had been obtained.

Since 1947 there has been a diminishing trend in the incidence of lupus and a tendency for the acute tuberculous type to show a relative increase.

It has been said that the patient with pulmonary tuberculosis does not tend to develop lupus and that the more acute tuberculous nasal disease is usually secondary to pulmonary disease. In this analysis, 16 per cent. of the lupus cases showed evidence of tuberculous chest infection and 22 per cent. of the acute tuberculous type showed active pulmonary tuberculosis, but the numbers did not permit more detailed analysis.

Summary

1. The case of a 12-year-old girl with acute tuberculous nasal disease is described. Phlyctenular keratitis and a primary lung complex were also present.

2. A rapid and satisfactory response to anti-tuberculous chemotherapy was obtained.

3. Thirty-four cases of tuberculous rhinitis over a ten-year period are briefly analysed from records and a trend away from the lupoid towards the acute tuberculous type noted.

We are grateful to Dr. N. W. Horne for criticism; one of us (D.T.K.) has to thank him for permission to take part in this publication. We also wish to record our indebtedness to Dr. Simson Hall, Dr. J. P. Stewart and Professor Crofton.

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GOLDEN JUBILEE DINNER

A DINNER to celebrate the fiftieth anniversary of the founding of the BRITISH JOURNAL OF TUBERCULOSIS AND DISEASES OF THE CHEST was held at Claridge's Hotel on Tuesday, January 24, Dr. Philip Ellman, Editor of the Journal, presiding. The dinner was arranged by the publishers of the Journal, and among those present were: Sir Russell Brain, P.R.C.P., Mr. Charles Read, P.R.C.O.G., Sir Clement Price Thomas, representing the Royal College of Surgeons, Dr. J. L. Livingstone, President of the Thoracic Society, Dr. W. E. Snell, President of the British Tuberculosis Association, Dr. J. E. Geddes, Chairman Joint Tuberculosis Council, Dr. G. F. Abercrombie, Chairman of the Council of the College of General Practitioners, Dr. T. F. Fox, Editor, *The Lancet*, Dr. Hugh Clegg, Editor of the *British Medical Journal*, Sir Heneage Ogilvie, Editor the *Practitioner*, Mr. Norman Barrett and Dr. J. G. Scadding, Editors of *Thorax*, Lord Moran, Sir Arthur MacNalty, Sir Adolphe Abrahams, Sir John Charles, Sir Daniel Davies, Sir Philip Manson-Bahr, Sir Weldon Dalrymple-Champneys, Sir Robert Young, Prof. John Crofton, Prof. Robert Knox, Prof. Alan Moncrieff, Dr. G. E. Godber, Ministry of Health, Dr. J. A. Scott, Medical Officer of Health for the London County Council, Mr. A. L. d'Abreu, Dr. Clifford Hoyle, Dr. F. H. Young, Dr. L. E. Houghton, Dr. Walter Levitt, Dr. Peter Kerley, and all the British members of the Editorial Board. Apologies were received from all the Dominion members of the Editorial Board, and Dr. Walsh McDermott, Editor of the *American Review of Tuberculosis*.

SIR ROBERT YOUNG, C.B.E., proposing the toast of "The British Journal of Tuberculosis and Diseases of the Chest" said that a golden jubilee invariably commemorated outstanding achievements, and this was no exception. It required great courage, vision and enthusiasm on the part of the first Editor, Dr. Kelynack, and the publishers, to start a Journal in a special field in 1906, when specialisation was at a very early stage of evolution. There were three special chest hospitals at the time, run for the most part by physicians attached to general hospitals. From the first number the Journal was approved of, and supported by, the chief specialists in tuberculosis and by the masters of medicine of the time. Sir Clifford Allbutt, then the *doyen* of the profession, contributed to it, and Sir Robert Philip wrote reiterating his faith in tuberculin. Sir Samuel Wilkes lauded the value of fresh air.

Dr. Kelynack was Editor for twenty-seven years. He was followed by Lancelot Burrell, whose early death was a great loss to the Journal. Dr. Clifford Hoyle succeeded him, and he recognised that its scope should be enlarged to include other diseases of the chest. All these Editors had maintained the critical and philosophical character of the publication. To give a list of its contributors would be to give a list of the authorities on chest diseases.

There were still problems confronting the speciality; the further development of the antibiotics, the necessity for discovering methods of securing lasting immunity and the question of the chronic open case, but in view of the past record of the Journal he was confident that these problems would receive the attention they deserved.

GOLDEN JUBILEE DINNER

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Turning to the present Editor, Dr. Philip Ellman, Sir Robert said that he had a wide experience of chest diseases from the clinical, pathological and administrative points of view. He brought great enthusiasm and industry to any work he took in hand. His writings showed that he had a critical faculty with a wide range and perspective, all of which contributed to the success of the Journal. As long ago as 1931 he wrote suggesting the reorganisation of the tuberculosis dispensaries into chest clinics, enlarging their scope and usefulness, and these suggestions were carried out seventeen years later under the National Health Act.

Dr. Philip Ellman, responding to the toast of the Journal, said that: "our Golden Jubilee is adequate cause for this joyous celebration. We have, through the years, remained an independent Journal in the field of tuberculosis and thoracic medicine; not so specialised, however, as to fail to integrate our speciality with general medicine.

" Sir Robert Young has lived through our life history, and we were proud to celebrate his eightieth birthday with a special number of the Journal, and were honoured to have him, in his eighty-fifth year, as a principal contributor to the Golden Jubilee Issue."

Dr. Philip Ellman felt that Editors of the clinical calibre of Kelynack, Burrell and Clifford Hoyle, and publishers of the quality of West and Tindall, could not but enhance the prestige of any journal. It is true that medical journalism was not the main profession of these Editors, but they learned their art in the hard school of experience. He (Dr. Ellman) had learned, from his predecessors, the need for ruthless editing, but an editor must be jealous of the reputation of his journal and was bound to make both friends and enemies.

He agreed with Sir Clifford Allbutt that: "the man of science ought best to know that style and matter can no more be dissociated than skin and bone; but if we write clumsily, loosely or disjointedly, our thoughts are accordingly."

With Professor Charles Singer, that great scholar, scientist, and valued contributor to this Journal, might we not agree, said Dr. Ellman, that: " Humanities and the sciences are far from being as independent of each other as many suppose. If literary studies lead to clear and effective thinking in the domain of science, scientific studies ventilate and inform and vitalise literature. The separation of the two disciplines, especially in the adolescent stage of mental development, does an injury to both."

Sir John Charles, K.C.B., Chief Medical Officer of the Ministry of Health, proposing the toast of medical journalism, referred to the age in which The British Journal of Tuberculosis was founded as a golden age of medicine, commemorated in the splendour of the Journal's Jubilee cover. The discoveries and advances of that age had been faithfully recorded for posterity by the Medical Journalism of the time.

He went on to consider the ways in which it had given outstanding service in the recording of facts as they appeared to the contemporary eye and understanding, the projection and propagation of ideas and the reflection of the medical world of the age. These services were offered with zest, good humour and success. " The integrity and faith of British Medical Journalism have been in accordance with the Hippocratic canon, and a model to the world."

Dr. T. F. Fox, Editor of *The Lancet*, replying to the toast, was weighed down by the responsibility of being spokesman for so many other medical journalists, present in the flesh or in the spirit. According to a recent list, there were now at least 6,369 medical editors—a noble army which, marching four abreast in

companies, would take 48 minutes to pass the saluting-point. " But even then you would be seeing only the editors; and a journal is so much more than its editor." Sir John Charles had likened medical journals to granaries of knowledge. They could also be compared to ships, or to stalls in weekly or monthly markets. But most of all, perhaps, they resembled gardens. " Within their walls we plant and cultivate, prune and graft, and perpetually sweep and weed—trying to get things tidy for the days when our garden is thrown open to the public." Some journals specialised in only one kind of fruit or flower: others were like botanical gardens where almost any species might be found. In some, everything was drastically cut back in the hope of getting a few splendid blooms: in others, the plants grew as they pleased. Much depended on the gardeners, and these in their turn might be many or few, jobbing or whole time. When Browning said that " he is a fool who does not know how much the half is better than the whole-timer " he was no doubt thinking of consultants (he married a Miss Barrett of Wimpole Street). But his statement probably applied also to gardeners and medical journalists; and Dr. Fox expressed his admiration for those clinicians, pathologists and others who—like Clifford Hoyle and Philip Ellman—gave so much of their time and of themselves to this part-time work. " Nobody who has not tried it has any idea of what such editorship means; and its labours too often go unregarded, or are taken for granted. But they are in fact the greater part of medical journalism."

Dr. Fox then put in a plea for part-time as opposed to whole-time poets, and recited some reflections by his part-time muse on Sir Robert Young, Sir John Charles, Dr. Philip Ellman, and Messrs. Baillière, Tindall and Cox. In conclusion he bade " Heaven speed the work of the Brit. J. Tuberc."

Mr. R. F. West, also in acknowledgment, said that there were two parents of The British Journal of Tuberculosis, Dr. Kelynack and Mr. A. A. Tindall, who was present at the dinner. Dr. Hoyle bore the heat and burden of the days through the war when conditions were so difficult, and he had handed to Dr. Ellman a goodly heritage. It would be agreed, he thought, that Dr. Ellman had added lustre to an illustrious series of editors. The Journal was a credit to him, and to the medical profession.

Mr. West added that many messages of goodwill and congratulation had been received, and regrets for inability to be present. At a jubilee one could look back and see what had been accomplished, and surely never had so much been accomplished in fifty years in the world of medicine as in the lifetime of the Journal. There were still problems and difficulties to be faced and overcome, but medical journalism would continue to assist, as it had done throughout the years.

PLATE XIV

SIR ROBERT PHILIP HONOURED ON POSTAGE STAMP

By W. J. Bishop

There are many postage stamps of interest to the phthisiologist, especially among the sets issued on behalf of the Red Cross or of anti-tuberculosis funds. Some account of these stamps was given in an article in the October issue of this journal (1950, **44,** 108) in which it was noted that no British worker in tuberculosis had been commemorated on a stamp. Special interest therefore attaches to a recent Belgian stamp which bears the portrait of Sir Robert Philip, M.D., F.R.C.P. (1857-1939). So far as is known, Sir Robert Philip is the first physician practising in Great Britain to be honoured on a postage stamp. Only four British medical men have previously been portrayed on stamps and none of these practised in Great Britain or made any contribution to chest diseases; none of them was in fact honoured primarily for his medical achievements. The four doctors alluded to were Sir Wilfred Grenfell, the famous medical missionary (Newfoundland, 1941); Sir Charles Tupper, M.D., Prime Minister of Canada (Canada, 1927 and 1955); Sir Ferdinand von Mueller, M.D., F.R.S., the eminent botanist (Australia, 1948); and David Livingstone (Rhodesia and Nyasaland, 1955).

The Philip stamp (the 8+4 francs, brown-black) is one of a set of seven issued on December 5, 1955, for the benefit of anti-tuberculosis and other charitable funds. Sir Robert Philip was the first to apply the scientific discoveries of Koch and his successors in the form of a co-ordinated scheme for the control of tuberculosis. In 1887 he opened the first tuberculosis dispensary in the world in Bank Street, Edinburgh. It is fitting that this great pioneer should receive a place in the philatelic portrait gallery in the company of Laennec, Auenbrugger, Skoda, Koch, Villemin, Calmette, and other immortals.

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REVIEWS OF BOOKS

Transactions of the 14th Conference on the Chemotherapy of Tuberculosis. Transactions of the 14th Conference Veterans Administration, Washington. Army, Navy Dept. of Med. and Surgery. February 1955. Pp. 556. Illus.

The Report of the Transactions of the 14th Conference of the United States Veterans Administration is devoted to the chemotherapy of tuberculosis. It makes very interesting reading for their colleagues working in this country, as it gives a bird's eye view of what those in the United States are doing and thinking. As in all these conferences, the quality of the papers varies, but on the whole the standard is high. Several reports give the results of pooled research schemes under the Veterans Administration which has been going on for some three years. Especially interesting is the conclusion that there is little difference in the results obtained by the use of any two of the principal antibiotics, streptomycin, PAS and isoniazid, though the results of the streptomycin and PAS régime are slightly inferior in producing cavity closure and negative sputa. What is essential, as workers in Great Britain have also found, is for treatment with chemotherapy to continue for at least twelve to twenty-four months, and possibly longer. Several papers on the results of chemotherapy for genito-urinary tuberculosis show that sterilisation of the urine can be obtained in nearly all cases of renal tuberculosis. All three drugs were used simultaneously, and their use continued for years. It is suggested that nephrectomy as a routine measure is obsolete. Several papers are given on the newer, less well established drugs, including Pyrazinamide, Cycloserine, Tetracycline, Viomycin and Ethyl-1-cysteine. The efficacy of Pyrazinamide, best used in combination with isoniazid, seems to be clearly proved, but there is still much argument about the incidence of toxic effects on the liver. On the original dosage of pyrazinamide 50 mg. per kilo body weight, the incidence of hepatic damage is unduly high. If, however, the daily dose does not exceed 3 g., and its use is stopped as soon as carefully repeated liver function tests indicate change, its use seems justifiable in desperate cases. Cycloserine gave very favourable results in a group of 37 cases, which included a high proportion of drug-resistant patients. No advantage was obtained by the simultaneous use of other antibiotics, and the toxic effects are not important. The use of resection for apparently successfully treated cases was discussed at length. " Randomised " investigation on the results of solid lesions after drug therapy (33), compared with similar cases (26) without resection, gave an equal number of relapses. It would be very interesting to compare the U.S.A. figures with those quoted by Sir Geoffrey Todd in his Marc Daniel lecture, when he described 230 cases of resection, none of whom has yet relapsed. It was most refreshing to note that several speakers suggested that results drawn from large-scale investigations cannot be applied successfully in a rule-of-thumb method to individual patients.

F. H. Young.

The Therapy of Skin Tuberculosis. By GUSTAV RIEHL and OSWALD KÖPF (Trs. Ernest A. Strakosch). Oxford: Blackwell Scientific Publications. 1955. Pp. viii+247. 50s.

The advent of high-potency Vitamin D, Isonicotinic Acid Hydrazide and Streptomycin has so simplified the treatment of cutaneous tuberculosis that the whole subject can easily be dealt with in one chapter of a work devoted either to tuberculosis or to dermatology.

This little book, which is difficult to read owing to the stilted language of the translation and the fact that its pages are frequently thickly peppered with references, deals in considerable detail with every form of therapy ever considered for skin tuberculosis. The sooner most of these are forgotten the better. In common with all dermatologists the writers conclude that Isonicotinic Acid Hydrazide (INH), either alone or in combination with Vitamin D, is the treatment of choice in skin tuberculosis, but curiously they devote only six pages to it. Though difficult to isolate, there is some good material in the chapter on Vitamin D.

There is a list of over 300 references at the end of the book, unfortunately many of them have no bearing on the subject which is the title of this work.

JOHN FRANKLIN.

Klinische Elektrokardiographie. By Dr. MAX HOLZMANN. Stuttgart: Georg Thieme Verlag. 1955. Pp. 687. Illus. D.M. 80.

Dr. Holzmann of Zurich is well known for his work in electrocardiography. This book is an extremely full treatise on the subject, including all the minutiæ of recording and translating electrocardiograms. It discusses not only the use of standard leads but also the value of œsophageal and intra-cardiac electrocardiograms. Vectorcardiography is fairly fully discussed.

In this book, as in some other similar monographs, the technical detail provided is probably a little disproportionate to clinical application and patient management. Also, there is sometimes too much stress on the use of the electrocardiogram in conditions where it can only, at best, give rather vague solutions; for instance, one is always happier to have the results from a flame photometer than an electrocardiogram in electrolytic disturbances.

It would have been nicer to have had a slightly fuller section on electrocardiography in acquired valve disease, especially mitral stenosis.

The illustrations are fairly clear, although in some electrocardiograms the time marker is difficult to see. There are many references, which are reasonably international, although there is, probably of necessity, an accent on literature in the German language.

It is not a book for the student, or even for the physician interested in cardiology, but a cardiologist who is interested in the extreme detail of his subject would enjoy it.

RAYMOND DALEY.

Les Bacilles de Koch Incomplètement Évolués dans l'Infection Tuberculeuse. By L. NÈGRE and J. BRETEY. Masson et Cie. 1955. Pp. 90.

The authors refer to the work of Calmette and Valtis upon the benign type of tuberculous infection produced by the injection of a filtrate of tuberculous tissue, and they claim to have proved that the original explanation is incorrect. According to the older view the inflammatory changes which result from this injection are due to the transfer of tuberculosis by means of a virus, but

the authors claim that the filtrate contains a "juvenile" form of tubercle bacillus with a low lipoid content and minimal virulence. The very young forms of the bacillus do not cause the same tissue reactions as do the more mature organisms, and they consider that the presence of these organisms explains many of the phenomena of the dissemination of tuberculosis by the blood stream.

Heures Internationales dans la Lutte contre la Tuberculose. By ÉTIENNE BERNARD. Masson et Cie. 1955. Pp. 90.

Etienne Bernard is the Secretary-General of the International Union for the prevention of Tuberculosis and, in this capacity, he travels the world giving addresses to the local associations of the countries which he visits. Naturally his lectures have a local flavour, but all have a theme of hope for the future. Tuberculosis mortality is declining in all civilised countries and we must increase our efforts to stamp it out completely. This volume contains the substance of addresses given in cities as far separated as Atlantic City and Madrid, and they contain the gospel of a man who is an expert on tuberculosis.

JAMES MAXWELL.

Experimental Tuberculosis, Bacillus and Host (with an Addendum on Leprosy). Ed. G. E. W. WOLSTENHOLME and MARGARET P. CAMERON. (Ciba Foundation Symposium.) London: J. and A. Churchill Ltd. 1955. Pp. xii+396. Illus. 42s.

This book is a report of the proceedings at a symposium on experimental aspects of tuberculosis organised recently in London by the Ciba Foundation. Those taking part were drawn from the leading authorities on the laboratory background to tuberculosis on both sides of the Atlantic, and the veritable galaxy of talent represented is indicated clearly by the list of contributors at the beginning of the book.

As might be expected from the title, this is not a book for the clinician, but the ingenuities displayed in the methods of approach to the many problems underlying tuberculous infection should provide a fascinating study for anyone with an enquiring mind. The essential object of the symposium was an enquiry into the fundamental nature of the tubercle bacillus and of the host reactions to it, but whether or not the average reader will have a clearer understanding of these matters after reading the book is open to conjecture, since the complexities of the subject revealed by searching enquiry may tend to confuse rather than to clarify. For the specialist there is much of interest in the fields of biochemistry, serology and tissue responses. References to chemotherapeutic problems are conspicuous by their almost complete absence, with the exception of a matter of considerable topical interest, namely the comparative avirulence for certain animals of some strains of tubercle bacilli resistant to isoniazid.

Perhaps the most valuable feature of all in this book is the full report given of the discussion which took place after each contribution. All too often, when one reads an article in a journal, a number of questions, as well as criticisms, come to mind which one would like to put to the author. In the discussion sections of this symposium many such questions are put and answered and the experiences of other experts in the field are described. In this way many loose ends are tied up and the value of each contribution is greatly enhanced.

J. ROBERT MAY.

Whys and Wherefores in Tuberculosis. By GEORGE DAY. (The National Association for the Prevention of Tuberculosis.) London. 1955. Pp. 44.

This small book is full of clarity and common sense about tuberculosis and will appeal to the layman. A brief epidemiological history of the disease is followed by a chapter on resistance. The basic principles of treatment are described, the salient points being underlined by touches of humour. The present position with regard to the controversial question of B.C.G. is summarised most aptly.

Any patient would surely be stimulated by this book, and it can be thoroughly recommended.

Rehabilitating the Tuberculous in England and Wales. National Association for the Prevention of Tuberculosis. 1955. By MURIEL OWEN-DAVIES. Pp. 71.

This is a factual survey of the manner in which rehabilitation of the tuberculous is handled in this country. It is a depressing picture in many ways and reflects badly on local authorities, many of whom appear to have ignored the permissive powers allowed them under Section 28 of the National Health Service Act. It reflects badly, too, on the machinery for making patients aware of such facilities as are available and presents a strong case for the provision of properly trained almoners in chest clinics. On the positive side, however, it is pleasant to learn that there are so many sources to be tapped, and it is hoped that these will be exploited to the full by chest clinics and local authorities.

This is a useful book for reference, and it is hoped that it will stimulate the provision of a better rehabilitation service in the future.

Aids to Thoracic Surgical Nursing. A complete Textbook for the Nurse. (Nurses Series.) By DOREEN NORTON. London: Baillière, Tindall and Cox. 1955. Pp. 232. Drawings and Plates. 7s. 6d.

This admirable new addition to the " Nurse's Aids " series is surely a " must " for those about to take up thoracic surgical nursing, and an excellent and refreshing revision book for those already so engaged. Here the whole field of this specialised branch is described lucidly and concisely. Sufficient line diagrams and a few well-chosen X-ray plates illustrate the text, and the whole work is completely up to date.

Apart from its other excellencies its greatest recommendation is that throughout the text we are never allowed to forget the patient—his anxieties, his difficulties and his discomfort—and the important rôle that the nurse plays in guiding him through what is a tremendous ordeal, both physically and mentally.

AUDREY HANSON.

BOOKS RECEIVED

The following books have been received and reviews of some of them will appear in subsequent issues.

Subphrenic Abscess. By H. R. S. Harley. Oxford: Blackwell Scientific Publications. 1955. Pp. xi+216. Illus. 35s. net.

Chest Clinic Design. Report of the NAPT Architectural Committee. London and Dunstable: Waterlow and Sons Ltd. 1956. Pp. 108. Illus. 12s. 6d. net.

Brompton Hospital Reports. Volume XXIII. England: Gale and Polden Ltd., Aldershot. 1954. Pp. ix+326. Illus. 15s. net.

Tuberculosis Index and Abstracts of Current Literature. NAPT. Vol. 10. No. 4. December 1955. Pp. 200. 25s. per year.

Causal Factors in Cancer of the Lung. By Carl V. Weller. Oxford: Blackwell Scientific Publications. 1956. Pp. viii+113. 21s. 6d. net.

Services for the Disabled. London: (Ministry of Labour and National Service) H.M. Stationery Office. 1955. Pp. 88. Illus. 4s. 6d.

Tuberculosis Control in Manitoba 1954. Annual Report of the Sanatorium Board of Manitoba, Winnipeg, Manitoba. Pp. 56. Illus.

Sigmund Freud: Life and Work. Volume Two. Years of Maturity. By Ernest Jones. London: The Hogarth Press. 1955. Pp. 534. Illus. 30s.

Tuberculosis in the Army of the United States in World War II. By Esmond R. Long and Seymour Jablon. V. A. Medical Monograph. 1955. Pp. viii+88.

Diseases of the Chest. By H. Corwin Hinshaw and L. Henry Garland. Philadelphia and London: W. B. Saunders Co. 1956. Pp. x+727. Illus. 105s.

Chest X-ray Diagnosis. By Max Ritvo. London: Henry Kimpton. 1956. Pp. 640. Illus. £6 net.

Pulmonary Circulation and Respiratory Function: a Symposium held at Queen's College, Dundee. Great Britain: D. C. Thomson and Co. Ltd. 1956. Pp. 44. Illus. 12s. 6d.

Les Fondements Anatomo-radiologiques de L'investigation Pulmonaire. By F. Kovats Jun. and Z. Zsebok. France: Masson et Cie. 1955. Pp. 336. Illus. 8,000 fr.

Ergebnisse der Gesamten Tuberkuloseforschung. Band XIII. Stuttgart: Georg Thieme Verlag. 1956. Pp. viii+659. Illus. DM. 96.

Segment und Lungentuberkulose. By E. Haefliger and G. Mark. Berlin, Gottingen, Heidelberg: Springer-Verlag. 1956. Pp. v+217. Illus.

Tagungsbericht zum 7. Kongreß der Süddeutschen Tuberkulosegesellschaft Zusammen mit den Südwestdeutschen Kinderärzten in Lindau (10.-12. *Juni* 1955). Edited by H. Brügger. Stuttgart: Georg Thieme Verlag. 1956. Pp. 99. DM. 6.

REPORT

N.A.P.T.

Mass Miniature Radiography Meeting

At a meeting organised by the NAPT on Friday, April 13, 1956 at BMA House, London, under the chairmanship of Sir Geoffrey Todd, Professor Manoel de Abreu of Rio de Janeiro, the world originator of mass radiography, described the first mass radiography survey, in 1937, when for the first time large-scale diagnosis became possible. Professor de Abreu felt that ten mass radiography units per million people were necessary to examine the entire population. Examination should be compulsory, and repeated yearly, or even twice yearly.

Dr. C. M. Smith, County Medical Officer of Health, Northamptonshire, gave some interesting facts on tuberculosis in the boot and shoe trade, which in the 1940's had an incidence of 6·19 per 1,000 examined. This fell in five years to 1·45, largely due to the discovery of chronic carriers. The co-operation of the boot and shoe trade (both Unions and Manufacturers) and of the Tuberculosis Care Committees was valuable in obtaining a high acceptance rate for M.R. examinations. Mass radiography, concluded Dr. Smith, was one of the most important instruments in the prevention of tuberculosis ever placed in the hands of Medical Officers of Health.

NOTES AND NOTICES

FOURTH INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS

Cologne, Germany, August 19-23, 1956

The Fourth International Congress on Diseases of the Chest of the American College of Chest Physicians will be held in Cologne, Germany, from August 19 to August 23, 1956, under the patronage of the Federal Chancellor, Dr. Konrad Adenauer.

The main subjects which will be discussed at the Congress, deal with the problems of coronary diseases (diagnosis, patho-physiology and surgery), industrial diseases of the chest, tuberculosis, lung and heart function and tumours of the mediastinum. Several outstanding foreign and German scientists and clinicians will present papers on these subjects.

NAPT SCOTTISH POST-GRADUATE TRAVELLING FELLOWSHIP

The Scottish Branch of the National Association for the Prevention of Tuberculosis is offering, for the second time, a Post-graduate Travelling Fellowship, value £250, to encourage a wider knowledge of modern methods of tuberculosis control among Scottish Chest Physicians.

Full details may be obtained from the Scottish Secretary, NAPT, 65, Castle Street, Edinburgh, 2. The closing date for receiving applications is June 30, 1956.